VOL. CLXII, No. 3 SEPTEMBER, 1921 No. 594

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THE

AMERICAN JOURNAL OF THE MEDICAL SCIENCES

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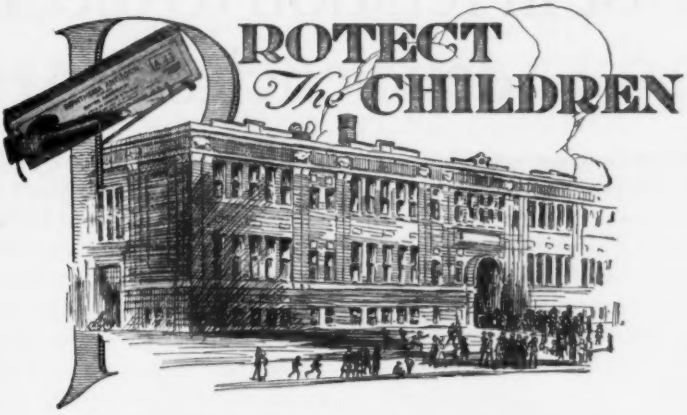

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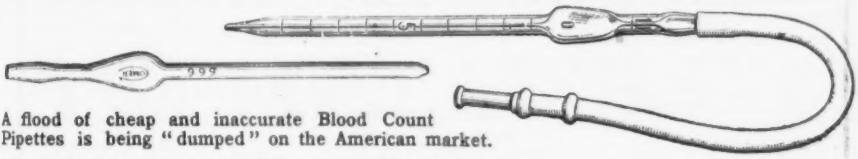

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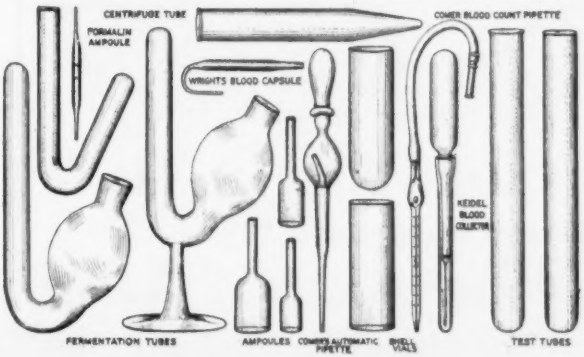

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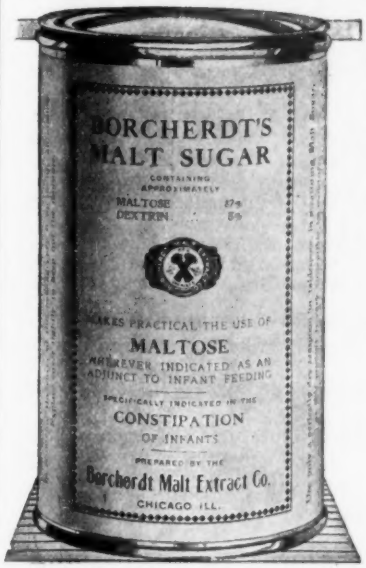

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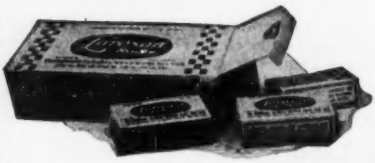

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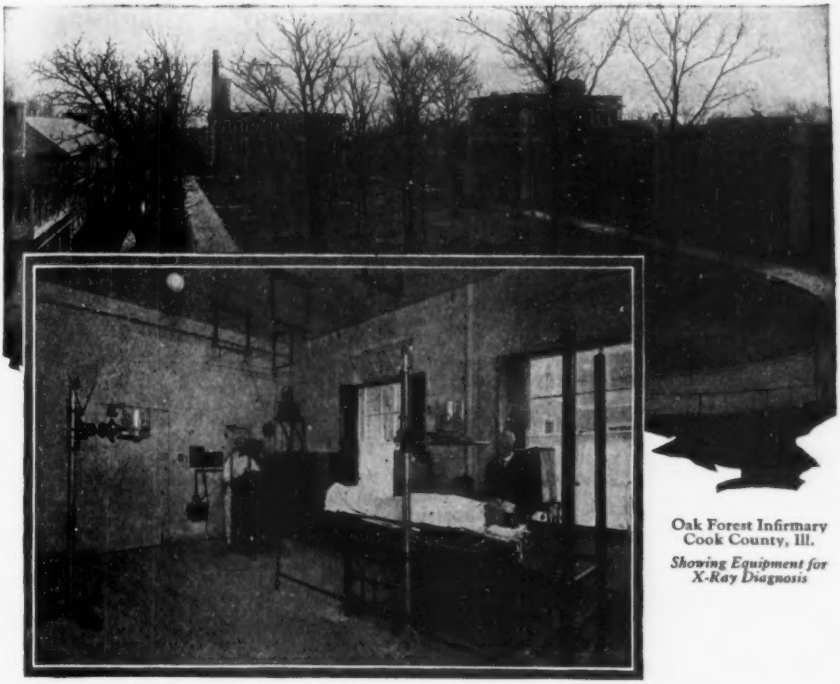

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ORIGINAL ARTICLES.

DIAGNOSIS AND CLINICAL MANIFESTATIONS OF CARDIO-SPASM ASSOCIATED WITH DIFFUSE DILATATION OF THE ESOPHAGUS.[1]

By Frank Smithies, M.D., F.A.C.P.,

CHICAGO, ILL.

ASSOCIATE PROFESSOR OF MEDICINE, COLLEGE OF MEDICINE, UNIVERSITY OF ILLINOIS; GASTRO-ENTEROLOGIST TO AUGUSTANA HOSPITAL.

I. **General Consideration.** Definition. A condition in which there occur diffuse dilatation of the esophagus with maintenance of the normal contour of the gullet and a varying degree of unusually strong and prolonged contraction or hypertrophy of the cardiac sphincter.

There may coexist hypertrophy of the muscle layers of the lower esophageal wall. The hypertrophy of the cardiac sphincter may be of but moderate extent, but when it is associated with powerful spasmodic or long-continued contraction there results transient or long-maintained, frequently complete obstruction to the passage of esophageal contents from the gullet into the stomach. Again, the hypertrophy of the cardiac sphincter may be advanced and then such hypertrophy may of itself result in functional stenosis of the cardia, whether or not there is the complication of associated spasm. In marked instances of the affection, the hypertrophy of the cardiac sphincter may resemble in degree such hypertrophy as is found at the pyloric sphincter in patients affected with the hyper-

[1] Read at the Twenty-third Annual Session of the American Gastro-enterological Association, Atlantic City, N. J., May 3 and 4, 1920.

trophic stenosis of infancy. Cases of "cardiospasm" described in which muscular hypertrophy of the cardiac sphincter could not be demonstrated at autopsy or operation would seem to be errors in diagnosis or faults in the observation of what actually constitutes muscular hypertrophy in a dilated, enlarged, static esophagus. There have been too few studies of the normal cardiac sphincter to permit comparison. During the past few years many papers have appeared purporting to describe "cardiospasm," but, in truth, such have dealt with instances of spasm at the cardia or of transient esophageal spasm, local or general.

NOMENCLATURE. It should be understood definitely that the terms "spasm at the cardia" and "cardiospasm" are not synonymous. Only the latter form of affection includes hypertrophy of the cardiac sphincter or the wall of the lower portion of the esophagus, combined with general, diffuse dilatation of the esophagus. "Spasm at the cardia" is a transient lesion of itself. It is not associated with uniform, diffuse dilatation of the esophagus until it has been so long existent or is of such constant maintenance as to produce esophageal changes not of a transient nature, particularly an associated, permanent dilatation of the gullet.

ETIOLOGY. In cardiospasm the dilatation of the esophagus would appear to be due to rather indefinitely understood causes. Rosenheim has suggested, as an explanation, primary atony of the muscular coats of the gullet. Kraus considers the condition due to the development of persistent, long-maintained spasm of the cardia, associated with paralysis of the circular muscles of the esophagus, the latter occurring as a consequence of degenerative changes in the vagi. Numerous authors, as, for example, Fleiner, Zenker and Sievers, maintain that dilatation results from a congenital predisposition on the part of the esophagus. Martin considers a primary esophagitis as an important factor. In addition there have been advanced other explanations, viz.: kinking of the esophagus at the cardiac opening; anatomical defects associated with the esophagus or the stomach, such as ulcer or carcinoma, and congenital or acquired asthenia. Plummer, following Mikulicz and Meltzer, is inclined to the opinion that, in addition to the changes occurring at the cardiac sphincter, there exists some disturbance of the nerve-muscle mechanism of the esophagus which may permit diffuse dilatation of the gullet irrespective of actual stenosis due to hypertrophy of the cardiac sphincter. Plummer emphasizes that in some patients there may be noted the occurrence of a habit of spasm at the cardia, and this, without anatomical, diffuse dilatation of the esophagus. Numerous such instances have found their way into the literature, misnamed "cardiospasm."

In our opinion it is likely that such extra-esophageal lesions as give rise to repeated, powerful, long-maintained contractions of the cardia are capable of producing the muscular hypertrophy of over-

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work; coincidently, this alteration in sphincter reflex-time secondarily disturbs the normal neuromuscular coördination in the esophagus above it. As a result, the overworked sphincter seems to develop its own independent contraction rate, and this of a duration beyond the normal time limits and out of the normal rhythm of the swallowing act. In such circumstances, the stimuli from above (formerly passing down to a cardiac sphincter, normally contracting and relaxing in appropriate time and with limited degree) are delivered in an uncoördinated fashion and at irregular time intervals, with little or no effect upon the systole and diastole of the cardiac sphincter. The initial overstimulation to the cardia would seem to be exerted by numerous anomalies. Such may be extra-esophageal or intrinsically esophageal. These stimuli may arise from the central nervous system, from the esophagus itself, from the diaphragm, the intrathoracic organs, from the stomach, duodenum, gall-bladder, appendix or other abdominal viscera. In some patients it would seem that more than usually powerful cardiac contractions are initiated by psychic upsets. However, it should be emphasized that cardiospasm is by no means an affection only of psychasthenics or of neurologically unstable individuals. While the initial cause of spasm at the cardia may produce a more active response in individuals who are psychically or nervously abnormally responsive to all stimuli, it should be recognized that in well-developed instances of cardiospasm the lesion which has to be dealt with is an anatomical one and not a mere functional disturbance. In these patients, in spite of the opinion to the contrary held by some clinicians, I believe there always exists a definite hypertrophy of the muscular cardiac ring (such as can be shown when skilled fluoroscopic study is made during the taking of food). With this is always readily demonstrable (although of varying degree) generalized dilatation of the esophagus. It is important that these facts be recognized because upon their realization depends the exhibition of proper methods of treatment. Patients affected with this lesion require more accurate therapeutic procedures than rest-cures, cessation from mental, psychic or physical overactivity, quieting medicines, Christian Science, osteopathic hocus-pocus and the like.

Structural Changes in the Esophagus. The anatomical anomalies present in cardiospasm should be emphasized, viz.: hypertrophy of the cardiac sphincter, atypic cardiac contractures (powerfully spasmodic or abnormally persistent) and diffuse enlargement of the esophagus without local or general gross alterations of its contour. The effect of these anatomical changes is to cause dysphagia, imperfect passage of foods into the stomach and, generally, some degree of permanent esophageal retention. The quantity of retained food varies widely in different patients and in a given patient at various times during the study of his affection. The

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esophagus may retain from less than an ounce to as much as several liters of fluid or mixed food. Upon the patient, the systemic effects are those consequent upon slow or rapid starvation. The degree of malnutrition may be so pronounced and of such acute development as to suggest malignant disease or advanced cicatricial stenosis caused by peptic, luetic, tuberculous or traumatic ulcer of the gullet.

II. Material Studied. During the past seven years 76 instances of cardiospasm associated with diffuse dilatation of the esophagus have come under my observation. Tabulated records of 47 of these cases are available for study.

Sex. Of the 47 cases there were 25 females and 22 males. This approximate equality of the sex ratio is rather striking in view of the prevalent opinion among practitioners that females are much more likely to be affected than are males.

Age. The average age for the series was 39.2 years; the youngest case was aged nineteen and the oldest seventy years. It is thus seen that true cardiospasm is a disease common to midadult life, the majority of instances occurring between twenty-five and thirty-five years.

Occupation. Occupation appears to play a very small part as an etiological factor, but the ailment seems to be relatively common in those individuals who are very active, physically and mentally. Temperament has been rather unduly emphasized in its relation to the initiation of cardiospasm. While it is true that some of these patients are delicately balanced psychically, yet a goodly number are of what one would call stable temperament.

Ailments previous to the onset of cardiospasm, with a few exceptions, appear to have little bearing with regard to causing the affection. It was noticed in our series that in 8 instances frequently recurring attacks of bronchitis or asthma were associated with dyspepsia and ultimately with dysphagia. These severe coughing spells might be a not unimportant factor in causing cardiac irritation and neuromuscular fatigue of the diaphragm. There were 3 instances of gastric ulcer proved by laparotomy, but the cardiospasm was in no way influenced by the operative procedure upon the stomach. In but 7 instances did shock, fright or acute fatigue precipitate the symptoms (2 were neuroses). Excessive smoking, particularly of cigarettes, was observed in 5 cases. This might offer an interesting etiological suggestion to those who attribute cardiospasm to vagus malfunction.

Mode of Onset. In but 17 instances the affection with the associated dysphagia was acute in its inception (36 per cent.). In 30 cases (74 per cent.) the affection appeared gradually and was not infrequently punctuated by attacks of exaggerated distress.

Duration of All Symptoms. This averaged for the series 5.6 years and ranged in the individual cases from three months to twenty years. The degree of dysphagia or esophageal retention not infre-

quently bore no relation whatever to the time that symptoms had been present. Not rarely, esophageal retention of as great as 1000 c.c. arose in individuals who had been ill for less than a year (9 cases).

The duration of the presenting trouble averaged for the series 4.2 years, with a range in the individual cases of from two months to twenty years.

DYSPHAGIA is not commonly painful. Usually there is a sensation of fulness or tension beneath the sternum, a feeling of tightness or a discomfort often described as "crowding of the heart." There may be dyspnea or cough. The first swallows of food may produce the uncomfortable sensation. It is of diagnostic significance to know that liquid foods are more prone immediately to bring about distress than are solids. In this way the type of dysphagia differs strikingly from that common to various forms of anatomical stenosis (ulcer, cancer, trauma, etc.) along the course of the esophagus. There are instances, however, in which the swallowing-act at once excites sharp cramp-like pains, usually located beneath the xiphoid or along the spine, from the ninth to the twelfth dorsal vertebræ. The pain may be at first sufficiently acute to cause incapacitation and then may be followed by intermittent or continuous gripping, binding or a "sticking" type of discomfort.

In our series of patients there was *constant* dysphagia in 45 cases. There was dysphagia to *fluids only* in 21, to *solids only* in 14 and to *all foods* in 12 cases.

Dysphagia is nearly always accompanied by *vomiting* or spasmodic food regurgitation so long as esophageal muscle tone remains good. A fairly characteristic and differential feature of the vomiting is that it is usually sudden, frequently explosive and very often occurs shortly after the ingestion of food. Liquids are more liable to produce sudden, copious emesis than are solids; in fact, the ingestion of soup or fluid at the early part of a meal may bring about spasmodic emesis of such sudden and forceful nature that the individual is compelled to rush hastily from the table to avoid accidents. This prompt vomiting of liquids is frequently aggravated by the fact that, but rarely, in general practice is the lesion of cardiospasm recognized. To the average physician a dysphagia presumably indicates a liquid diet, and he accordingly orders such. Solids or partly solid foods are generally well borne, particularly in the early stages of cardiospasm. The constant attempt to take liquids is followed promptly by vomiting, lack of nourishment and malnutrition, and doubtless added damage to the weakened esophageal wall. The patient frequently finds this out himself and refuses to follow his physician's instructions when liquid diet has been urged. In advanced cardiospasm practically all the food taken may be vomited within an hour or two following its ingestion, or if dilatation of the esophagus is pronounced, morning retention-vomiting is common and constant.

esophagus may retain from less than an ounce to as much as several liters of fluid or mixed food. Upon the patient, the systemic effects are those consequent upon slow or rapid starvation. The degree of malnutrition may be so pronounced and of such acute development as to suggest malignant disease or advanced cicatricial stenosis caused by peptic, luetic, tuberculous or traumatic ulcer of the gullet.

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DYSPHAGIA is not commonly painful. Usually there is a sensation of fulness or tension beneath the sternum, a feeling of tightness or a discomfort often described as "crowding of the heart." There may be dyspnea or cough. The first swallows of food may produce the uncomfortable sensation. It is of diagnostic significance to know that liquid foods are more prone immediately to bring about distress than are solids. In this way the type of dysphagia differs strikingly from that common to various forms of anatomical stenosis (ulcer, cancer, trauma, etc.) along the course of the esophagus. There are instances, however, in which the swallowing-act at once excites sharp cramp-like pains, usually located beneath the xiphoid or along the spine, from the ninth to the twelfth dorsal vertebræ. The pain may be at first sufficiently acute to cause incapacitation and then may be followed by intermittent or continuous gripping, binding or a "sticking" type of discomfort.

In our series of patients there was *constant* dysphagia in 45 cases. There was dysphagia to *fluids only* in 21, to *solids only* in 14 and to *all foods* in 12 cases.

Dysphagia is nearly always accompanied by *vomiting* or spasmodic food regurgitation so long as esophageal muscle tone remains good. A fairly characteristic and differential feature of the vomiting is that it is usually sudden, frequently explosive and very often occurs shortly after the ingestion of food. Liquids are more liable to produce sudden, copious emesis than are solids; in fact, the ingestion of soup or fluid at the early part of a meal may bring about spasmodic emesis of such sudden and forceful nature that the individual is compelled to rush hastily from the table to avoid accidents. This prompt vomiting of liquids is frequently aggravated by the fact that, but rarely, in general practice is the lesion of cardiospasm recognized. To the average physician a dysphagia presumably indicates a liquid diet, and he accordingly orders such. Solids or partly solid foods are generally well borne, particularly in the early stages of cardiospasm. The constant attempt to take liquids is followed promptly by vomiting, lack of nourishment and malnutrition, and doubtless added damage to the weakened esophageal wall. The patient frequently finds this out himself and refuses to follow his physician's instructions when liquid diet has been urged. In advanced cardiospasm practically all the food taken may be vomited within an hour or two following its ingestion, or if dilatation of the esophagus is pronounced, morning retention-vomiting is common and constant.

The vomitus consists commonly of material whose appearance resembles that of food as eaten. It is alkaline in reaction, usually contains much mucus, rarely lactic acid or blood and may have a high, bacterial content. At times vomiting is "delayed" and only when a large meal is taken at night is emesis produced. At that time, food eaten at breakfast or even the night before may be vomited unchanged. Sometimes the vomitus is copious at night and prevents proper rest and sleep. A few cases of even marked cardiospasm do not manifest actual vomiting, but there is constant belching, bad taste in the mouth, eructations of food and, frequently, copious regurgitation of ill-tasting fluid, food or mucus. Sometimes nausea is pronounced and there occurs remarkable increase in the secretion of saliva. This may indicate central irritation of the salivary glands. Even when some food passes the cardia the regurgitation of frothy, thick, tenacious mucoid material is apt to be annoying, particularly when such occurs toward evening. Consequent upon the vomiting appear evidences of lack of fluid in the tissues, constipation, diminution of urine output, headaches, dizziness and anemia.

In this series of cardiospasm patients, 31 vomited daily (frequently many times during the day). In 22 cases retention-vomiting was observed. Frequently, food (fruit skins, pieces of tomato, meat, lettuce, milk-clots, etc.) was retained in the lower part of the dilated esophagus for as long as a week. In 17 of our patients the vomiting was projectile. In such cases it was a common experience that patients began vomiting as soon as food was swallowed. There was vomiting of blood in 14 cases. This hematemesis, seemingly, bore relationship to dilated or varicose veins in the lower esophagus, although one could not always be certain that ulceration had not taken place in some portion of the esophageal wall where varicosities were not present. In one case the hematemesis appeared to be definitely "vicarious," inasmuch as it occurred on two occasions just before menstruation.

Regurgitation, without actual vomiting, was especially annoying in fifteen patients. This regurgitation was generally uncontrollable and the regurgitant food-mass was frequently very copious in quantity and of a foul, sickening odor. There were patients in which periods of intermittent regurgitation preceded cycles of exhausting vomiting.

Miscellaneous Clinical Symptoms. Weight loss was experienced by all our patients. It averaged, for the series, 28.2 pounds. In individual cases it ranged from ten to as much as eighty-two pounds. The appetite was stated as being lessened or as being poor in 44; 9.5 per cent. patients experienced pronounced anorexia. Normal bowel movements occurred in 47 per cent. In the remaining cases there was obstinate constipation. This constipation seemed to be due largely to insufficient quantities of food or fluid passing the cardia into the stomach and bowel.

III. Special Diagnostic Maneuvers.—In true cardiospasm, an unguided *stomach tube* passed into the esophagus usually excites free food regurgitation about the tube and the spasmodic emesis of much food and liquid through the tube. The tube may be generally passed freely as far as the normal cardia, but there it meets an elastic resistance. This resistance is occasioned either by the tube's impinging on the distended esophageal wall and depressing its lower sixth into a sac-like pouch, or by pronounced and persistent contracture of the cardiac sphincter. In only but a few not well-established instances of the affection does the cardia lie in a line direct from the pharynx and thus allow an unguided stomach tube to be passed to it, and then, upon exertion of pressure, admit of the cardia's being forced, the tube being carried into the stomach. If the tube is guided upon a silk cord to the cardia (as suggested by Mixter, of Boston, seventeen years ago and emphasized by Henry Plummer clinically), it can be carried direct to the cardia, and, provided the tube is a stiff one, can, with the exertion of a moderate degree of force, be passed into the stomach. The "giving way" of the tight, elastic cardia can be felt as the stomach tube passes the hypertrophied or permanently contracted sphincter.

If not guided to the cardiac orifice by a cord, a *bougie* passed into the esophagus traverses the lumen farther than the average distance of the cardia from the incisor teeth. Usually the olive may be passed considerably farther than normally and the unsuspecting manipulator may fancy that he is well beyond the cardia and that the olive lies in the stomach, it having passed the cardiac sphincter without the operator's knowledge. This mistake occurs as a result of the bougie's passing downward and to the right in the folds of the sac-like, pendulous lower esophagus. In such circumstances forcible pressure is dangerous: in our own experience one case of esophageal rupture occurred after the patient had been elsewhere "dilated by olives" for six months and the cardia was later divulsively dilated. At the autopsy it was found that at the lowest point of the dilated esophageal sac, and about two inches from the cardia, there were denudation of the mucous membrane, marked thinning of the wall of the esophagus and peri-esophageal inflammatory thickening. The area of the esophageal attenuation was about the size of a large olive, somewhat depressed, and lay in a straight line from the pharynx to the lowest part of the esophageal sac, but was out of the straight line from pharynx to cardia. In this patient, a divulsing dilator, guided upon a silk cord, passed freely into the cardiac orifice, but the increase in intra-esophageal pressure during dilatation was sufficient to cause rupture of the esophagus at the spot where repeated bouginage had weakened the walls.

Even in long-established, obstinate cardiospasm it is generally possible for a silk cord guide to pass from the esophagus into the stomach, but at times the cord may be held in the esophagus several

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days and may pass freely only when spasmodic contracture of the cardia has been minimized by the free use of atropin or of belladonna. However, unless the dilated esophagus be washed clean of retention contents silk cords may lie for weeks without passing from the gullet to the stomach.

An olive bougie of large size passes readily to the cardia upon a taut string; moderate pressure "forces" the sphincter and permits the bougie's passing into the stomach. Withdrawal of the bougie may be accompanied by a readily recognizable, elastic resistance. It is usually the experience that the bougie exerts little influence with respect to permanent enlargement of the cardiac opening or permanent relief of the dysphagia. It is quite as sensible to expect permanent dilatation of a cardia in cardiospasm by bouginage as it is to expect that a spasm of the anal sphincter will be relieved by frequent digital examinations. If the patient be examined at different times of the day or upon different days a variation in the amount of resistance at the cardia may be determined, but it is characteristic of the affection that at every examination there is resistance present.

The roentgen examination is of great aid in diagnosis but the evidence which it supplies is not infallible. Fluoroscopic observation and plate studies must be carefully interpreted in the light of clinical history, physical examination and examination of the esophagus by guided instruments.

Fluoroscopically when the patient swallows the opaque meal it will be seen that usually a small amount of the mixture immediately passes through the cardia into the stomach. In moderately well-established instances of the affection the cardia then closes quickly, with or without several, easily recognized, squirty contractions and continued ingestion of the opaque mixture results only in filling out the esophagus; practically nothing passes into the stomach. It can then be shown that the esophagus is uniformly dilated, that its wall is regular, that dilatation occurs along anatomical lines and that the cardiac end of the esophagus down to the hypertrophied sphincter presents no gross irregularities of contour. In shape such a dilated esophagus resembles, characteristically, a large lily-of-the-valley leaf, or is roughly pear-shaped. The dilatation may be enormous and extend so markedly throughout the entire length of the esophagus as to produce pressure upon the heart, the aorta or the trachea. The obstruction at the cardia may be absolute and may be maintained for hours or days until emesis or lavage results in an apparently reflex partial relaxation of the hypertrophied cardiac sphincter. Again, in moderately advanced cases esophageal retention may persist from a half to two hours and then the opaque meal passes in a jerky, spasmodic fashion, slowly through to the stomach. Even in these cases, however, one rarely finds that the esophagus completely empties itself within from two to six hours. In the early, incompletely established cases esophageal retention may be but a tran-

sient one. Fluoroscopically it is possible to observe alternate, spasmodic contractions and relaxations of the cardiac sphincter,

FIG. 1.—Lateral roentgenogram, showing bismuth meal retention in case of "cardiospasm." *A*, closed cardia, without malformation; *B*, diffusely dilated esophagus, normal contour maintained; *C*, anterior depression caused by aortic arch; *D*, shadow of heart. (Roentgenogram by Joseph Johnson.)

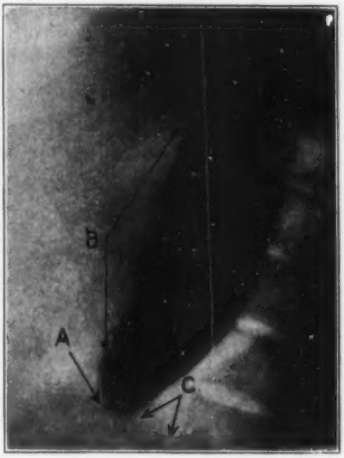

FIG. 2.—Lateral roentgenogram of bismuth meal retention in case of "cardiospasm." *A*, cardia, in contraction, without malformation, but with stenosis complete; *B*, diffusely dilated esophagus of rather marked degree, but contour normal; *C*, diaphragm line. (Roentgenogram by Joseph Johnson.)

associated with the intermittent passage of small amounts of the opaque meal from the lower esophagus into the stomach. The esophagus will thus empty in from a few minutes to an hour. Mild

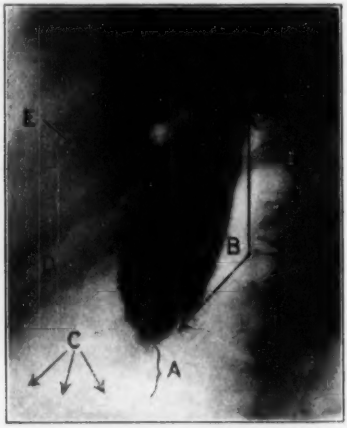

FIG. 3.—Lateral roentgenogram, showing retention of bismuth meal in a case of ring cancer involving the lower one-sixth of the esophagus, with complete stenosis. *A*, zone of cancerous involvement; *B*, dilated esophagus, proximal to cancer; *C*, diaphragm line; *D*, heart shadow; *E*, aortic arch. The lower portion of the esophagus has a contour resembling normal, and plate might readily be mistaken for one of "cardiospasm" if care is not exercised in locating the cardiac end of the esophagus in relation to the position of the diaphragm line and the gas shadow in the stomach. (Roentgenogram by Joseph Johnson.)

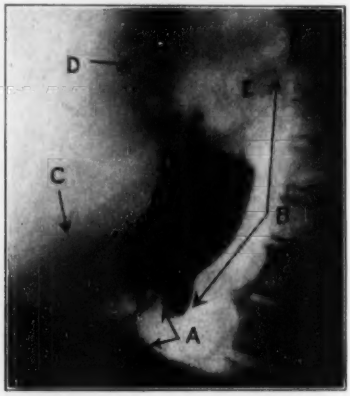

FIG. 4.—Lateral roentgenogram of retained bismuth meal in the esophagus, the cardiac end of which is stenosed by cancer of the nodular, cauliflower type. *A*, zone of cancer, irregularly canalized; *B*, dilated and partly filled esophagus; *C*, heart shadow; *D*, shadow of aortic arch; *E*, dilated, but not filled, esophagus, the dilatation extending above the tracheal bifurcation. (Roentgenogram by Joseph Johnson.)

instances of the affection are not generally associated with great sac-like esophageal dilatation.

In rare instances, fluoroscopy and roentgen plates fail to make the diagnosis, the roentgen findings seem characteristic for cardiospasm, but in the dilatation of the esophageal sac, ulceration, diffuse scirrhus carcinoma or lues may remain masked even until they have advanced sufficiently to produce extensive stricture or to cause death from metastasis. Not rarely, fluoroscopy clearly demonstrates torsion of the terminal esophagus with or without rather sharp angulation or displacement, usually to the left of the midline of the thorax.

In several instances of well-developed cardiospasm with diffuse dilatation of the esophagus I have noted unusual "doming" of the diaphragm. In these patients the diaphragm movements were atypic: degree of depression was unequal on the two sides, rates of downward movements were not equal on the two sides, *i. e.*, the diaphragm depressions were not synchronous and, locally, in the region of the hiatus there seemed to be a sort of "piling up" of diaphragm (local hypertrophy). Observation of the above phenomena has suggested to me that at times the fault primary in initiating cardiospasm lies in the muscle or serous layers of the diaphragm (inflammatory processes in the serous coverings of the esophagus, lungs, heart, diaphragm or a local myositis of the diaphragm itself), with resultant disturbance in the neuromuscular mechanism of the diaphragm, and, subsequently, of adjacent viscera with their correlated nerve supply.

It should be scarcely necessary to mention that fluoroscopy, conducted with the patient only in the anteroposterior position, can at its best give but incomplete information. Unless the patient is examined also laterally so that the course of and the anomalies in the esophagus are susceptible of complete exposure much of interest and of clinical usefulness will be lost. It is advisable to examine fluoroscopically during the swallowing act with the diaphragm depressed by deep inspiration, the breath being held and the diaphragm fixed during swallowing. The patient may be turned rapidly from the anteroposterior to the lateral ("quartering") position, and by this maneuver one may secure views of the lowest portion of the esophagus, of the sphincter, the contour, peristaltic activity and the position and shape of the diaphragm. For careful scrutiny of the terminal esophagus and the cardiac sphincter the fluoroscope's diaphragm should be closed to such point as will permit minute study of the esophageal contour inch by inch. Such procedure is necessary to detect or rule out ulcers, scirrhus carcinoma, etc., and to properly study the sphincter and its action. The successive employment of thin fluid and thick mush-like, opaque suspensions gives useful information relative to sphincter action, esophageal peristalsis, stasis, contour and degree of dilatation.

The patient should be examined at least on two successive days. The second study should be carried on after the exhibition of antispasmodic medicines to physiological tolerance. Only in this way can one determine the true condition existing at the cardia and the actual size of the esophagus. If this procedure were routinely followed, many "literature" cardiospasms would disappear—for many such are only "spasm at the cardia."

Roentgenograms should be made with the patient in the semilateral or "quartering" position as well as the anteroposterior. When plates are made with the patient in the semilateral position the entire esophageal contour may be delimited. In order to bring out the cardia and the lower portion of the esophagus it is advisable to have the patient drink as much of the opaque meal as he is able to, then clasp his hands high above his head and take a deep breath. The inspiration depresses the diaphragm and generally enables accurate visualization of the lower esophagus. The best roentgenograms are made with the patient standing with his left side next to the plate. When extensive esophageal dilatation is present, anteroposterior roentgenograms also should be made in order to determine the lateral limit of the esophageal sac and to demonstrate the degree of encroachment of the enlarged esophagus upon the heart, aorta and lungs. Such plates frequently demonstrate that the lowest limit of the dilated esophagus lies several inches below the level of the cardiac sphincter. This shows, vividly, how futile is the effort to pass bougies or tubes into the stomach without their being guided from pharynx to cardia by a swallowed silk thread. In patients in whom the cardiospasm is not far advanced, anteroposterior roentgenograms even may fail to indicate that the condition is present. In such circumstances the esophageal shadow is overlapped and hidden by the shadows of the heart, the aorta and the spine. Series of plates should be made before and after the administration of antispasmodic medicines (belladonna, benzylbenzoate, etc.). Such permit of interesting comparative studies and furnish valuable records of anatomical changes as the functions of the esophagus are restored by treatment.

Esophagoscopy. Inasmuch as in certain cases of cardiospasm the initiating fault lies in an esophageal lesion it would appear a proper procedure to explore by sight the entire esophageal mucosa from pharynx to cardia, that is, provided that one who is familiar with esophagoscopes and who knows the significance of what he sees is able to do the work. Much esophagoscopic work as done is worthless because the operator knows little of the appearance of the normal esophagus. In well-established instances of cardiospasm an actual view of the interior of an enormously dilated gullet and an anomalously acting sphincter is truly worth while if for no other reason than to satisfy one's curiosity. When some doubt exists respecting whether or no a cardiospasm is complicated by

scirrhus cancer, peptic ulcer, foreign body, gumma or extra-esophageal ailment, certainly, esophagoscopy is a justifiable procedure to clear up doubtful points in diagnosis even though it is annoying to the subject. A thoroughly cleansed esophagus, carefully administered intratracheal anesthesia and a good esophagoscope, such as the particularly ingenious Sussmann, greatly facilitate the procedure. When powerful contractures of the cardiac sphincter persistently recur, following most expert divulsive treatment, it would seem necessary always to perform esophagoscopy with the object of searching for and treating locally irritative mucosal lesions.

Prognosis. If the affection is properly managed, there is clinical and functional recovery in about 70 per cent. of even well-established instances of cardiospasm. Improvement occurs in 20 per cent. About 10 per cent. of the patients are not permanently benefited by any form of treatment at the most expert hands. The lesion seemingly resists all forms of therapy. In this class are patients extremely emaciated, instances of irritable esophagus where proper treatment cannot be carried out and very likely cases in which there is a congenital defect, or, as Plummer has emphasized, the persistence of a "habit of spasm." For these unfortunates, gastrostomy may be required to save or prolong life. If with cardiospasm there are such associated lesions as gastric ulcer or malignancy, gall-stones, appendix infection or ulceration or inflammation of the cardia or esophagus itself prognosis is seriously limited unless these lesions are amenable to appropriate medical or surgical treatment. Even after the restoration of the cardiac sphincter action, the esophagus may remain much dilated and permit food retention. However, it is surprising how dilatation of the esophagus may persist, and yet such is unaccompanied by troublesome dysphagia, provided the cardiac orifice is patent and the sphincter acts normally.

THE SPLEEN AND DIGESTION:

Study I.—The Spleen and Gastric Secretion.[1]

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The exact rôle of the spleen in digestion is not known. Numerous hypotheses have been advanced and much experimental work has

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The author wishes to acknowledge his indebtedness to Professor A. J. Carlson, University of Chicago, in whose laboratories the experimental portion of this work was done, and to express his gratitude to his brother, Charles F. Inlow, for assistance in many details of this study.

been done with contradictory results. Various conclusions arrived at have been:

1. The spleen is an endocrine organ with the function of influencing, in an obscure manner, some portion of the digestive apparatus by way of the blood stream or of activating one or more of the digestive enzymes by an internal secretion.

2. The spleen is a storehouse for the temporary reception of the products of protein digestion, much as the liver is for glycogen.

3. The spleen is merely a diverticulum of the portal system to receive the excess blood rushed to the splanchnic area during the digestive period and to act as an abdominal heart for supplying this blood to the stomach and other abdominal organs as needed.

The idea that the spleen must be of some significance in this regard has been prompted by the gland's intimate anatomic connections with the portal system, marked congestion and swelling observed during the digestive period, proportionately excessive atrophy during starvation and inanition, and by references by many experimental investigators, as well as many clinicians, to a state of hunger and voracious appetite after splenectomy.

The present study approaches the rôle of the spleen in digestion from the viewpoint of its relationship to the stomach, especially the effect of splenectomy on gastric secretion. All previous work on this aspect of the problem is foreign, and most of it given in publications not readily accessible; for this reason I am reviewing the literature in some detail.

Review of the Literature.

The spleen and stomach from the earliest times have been supposed to possess some close interrelationship. Stukeley in his most excellent dissertation on the spleen, published in 1723, definitely assigned to this organ as its second major function the duty of being an adjunct to gastric digestion, and admirably reviewed the tenets of previous authors. He approached the subject thus:

"But let us proceed to what I imagine one of Nature's primary purposes in the formation of this curious organ (spleen): That is, for an assistant of the great business of digestion or concoction of the aliment in the stomach; the first and highest importance of all others, for preservation and support of the individuum, the mainspring of the wonderful machine, rightly by Plato from Hippocrates called the primum mobile, alluding to the imagined first agent of the rotation of the huge celestial orbs. This is no new opinion but rather an old one, well started by the Ancients, but neglected by their successors, especially the Moderns. The divine Hippocrates, to whom scarce any truth was unknown, thought the office of the spleen was to help concoction, by drawing off the superfluous humidity from the stomach, whom Aristotle copies after. Others

supposed this assistance was performed by furnishing the stomach with its acid ferment, whence it excited hunger, stirring up the vis appetitrix. Aristotle made it, being a sanguineous organ, the concocter of the crudities that otherwise would offend the stomach. Some have thought the spleen's fancied melancholy useful to the stomach, by its acid, austere, styptic and astringent quality which contracted and strengthened the fibers thereof and enabled it the better to concoct and retain the aliment whilst digested and expel it afterward, as Galen says in the lion, leopard, bear, wolf, pard, etc.; and the Arabians fell pretty much into this notion, for they always thought it strengthened the stomach."

Stukeley was of the opinion that any common observer in anatomy naturally would be tempted to conclude that the spleen has some relation to the stomach when he found the one placed directly under the other, and with the intimate intercommunications by means of their common veins, arteries, nerves and connections that exist invariably in all creatures.

He was led to answer the questions why the principal bloodvessels of the stomach arise from the splenic artery in its direct route to the spleen and why vessels go immediately from the spleen to the stomach, as ordinarily do the vasa brevia, by formulating the theory that the spleen acts as a "heart to the stomach," that it is a magazine, diverticulum or necessary receptacle of the blood for the use of the stomach, ready, as occasions and emergencies require, to send plentifully of its supply into the gastric vessels, later when the blood is not needed there to receive it back again. This is of great service in a part that must so suddenly alter its dimensions, extend its bulk and contract itself in its great business of digestion as does the stomach.

However, this was not the only office wherein the spleen was subservient to the stomach, for (in common with Aristotle, Anonymous Graecus and Galen, who affirmed that the spleen assists in warming the stomach, and with the great Vesalius, who said *Lienem suo calore innato ac frequentibus quae illum intertexunt arteriis ventriculi concoctionem favere*) he advanced the opinion that the spleen by its proximity, great vascularity and timely congestion furnishes heat to the stomach. He asked "— does not nature proclaim its (spleen's) great eminence by its situation, being placed on the left side of the stomach where digestion is chiefly performed, and closing it up, as it were, like the door of a furnace, that it may have an equable warmth quite around so that the spleen alone in this single requisite of heat is apposed to all the rest of the bowels put together that encompass the stomach." He further adduced as proof of this assumption the "notorious" and "terrible" effects produced by eating ice and snow liquors in hot countries! Is this not in accord with the fancy entertained by the ancients "that creatures which drink much have larger spleens, whose business it is to warm the stomach against such a quantity of cold fluid"?

Stukeley's position can then be summarized happily in his conclusion "that if the stomach in the opinion of Q. Serenus deserves to be called *Rex totius corporis*, the spleen deserves to be called its viceroy."

The "immortal" Haller in reviewing hypotheses concerning a *secretio lienalis* mentioned the idea that had been advanced that the spleen elaborated an acid juice which, sent to the stomach through the vasa brevia, aided in digestion. He himself denied such a function. (*Lien non est acidus. Vasa brevia nihil a liene in ventriculum sani hominis vehere; et lange minus aliquid in arteriam remittunt.*)

Oken maintained that the gastric juice and chyme undergo a process of oxidation, and that the spleen in this respect holds a somewhat similar relation to the stomach to that which exists between the air and the lungs or the placenta and the fetus.

Finally, Burdach denied any relationship between the two organs because *aucune des hypothéses dans lesquelles on fait concourer ce viscere a la digestion, ne repose sur la moindre preuve.*

However, Baccelli has been credited generally with being father to the hypothesis of a distinct functional relationship between the spleen and the stomach, for he was the first scientifically to base his deductions on original clinical observations and anatomic studies. In 1868, at Rome, he gave his theory to the world in a discussion on malaria. In his extensive experience he had noted that during the prodromal and defervescent periods of paludism the patient frequently showed a voracious appetite; conversely, during a period of malarial cachexia a special dyspepsia intervened, resistant to all therapy. In the first instance only a soft evanescent splenic tumor was present, in the latter a lasting hyperplasia of more or less of the organ modified only by the amount of hyperemia. This dyspepsia was most marked toward albuminoid food material, and he found in the vomitus of the patients unchanged meat fibers, even after two or three days, indicative of impaired peptic activity.

Baccelli then carried on anatomic studies in which he demonstrated a definite gastrosplenic circulation. He found that the veins of the vasa brevia form five or six rectilinear canals, with intercommunicating smaller vessels, from the spleen to the cul-de-sac of the stomach, which are devoid of valves, so that the blood can pass in either direction; it may go at one moment to the stomach, at another to the spleen or remain in the interposed vascular system. These vascular connections he designated as *una piccola circolazione addominale*. The largest number of gastric glands are situated in the cul-de-sac at the area supplied or drained by these veins. The manner in which the blood streams of the vena coronaria sinistra and vena splenica are confluent he summed up as follows: *Difatti, dalla milza a capillari dello stomaco pe'vasi brevi- da'capillari dello stomaco alla vena coronaria sinistra- dallo stomaco pe'vasi brevi alla*

milza- dai capillari della milza alla vena splenica- dalla vena splenica e dalla coronaria sinistra al confluente. On the basis of this anatomic relationship Baccelli formulated the following hypothesis: Considering the large amount of carbon entering into the molecular composition of pepsin it seems likely that the spleen is deputized to furnish this material, in the form of carbonic acid, to the peptic glands for their proper function. The stomach dilated by the blood given it compresses the splenic vein against the vertebral column, obstructing thus the venous splenic outflow and causing still greater splenic engorgement, with the forcing of blood through the veins of the vasa brevia to the cul-de-sac of the stomach. Thus the *ragione d'essere* of the little venous abdominal circulation was explained, in which the carbonic acid was used in perfect antagonism to its rôle in the little thoracic circulation where it is eliminated.

Baccelli's anatomic research was repeated by Roseo in 1870 and confirmed in all particulars. Nothing further was done on the subject until 1901. In this year Tarulli and Pascucci, working in Luciani's laboratory, carried out a set of experiments on dogs in which they determined the digestive activity of the gastric juice before and after splenectomy. Gastric fistulas were made according to Claude Bernard's method. A preparatory meal, consisting of 500 gm. each of cooked meat and broth and 200 gm. of bread, was fed with the idea of exhausting the pepsin accumulated in the gastric glands. Sixteen hours later the mucous membrane of the stomach was washed out with isotonic salt solution and a secretory meal consisting of 100 gm. of cartilage and tendons given. The resulting secretion of gastric juice was collected and tested for peptic activity by placing 1 gm. cubes of coagulated egg white in 10 c.c. samples of pure juice for twenty-four hours at 39° C., the amount of digestion being determined by the loss in weight of the cubes after this period. The results obtained led Tarulli and Pascucci to the conclusion that the digestive power of the gastric juice is constantly decreased to a greater or less extent after splenectomy. Furthermore, they found that by feeding an infusion of congested spleen, that is, spleen excised five or six hours after a meal, the digestive power was increased again for from one to three days. From these results they assumed that during gastric digestion the spleen elaborates a pepsinogenic substance which is carried to the gastric glands through the blood stream and induces an increased amount of pepsin secretion.

Gallenga, in 1902, performed some digestive experiments on a patient splenectomized for a large blood cyst of the spleen. The spleen was large and hard and showed hyperplasia of the connective trabeculæ, with reduction of the tissue propria. The patient recovered from the operation, maintained a good appetite and had no subjective digestive disturbance. A month later Gallenga started his experiments with three test-meals: the Ewald (vegetable), Leube (vegetable and meat) and Ferrannini (meat). No determina-

tions were made preceding splenectomy. His results he summed up as follows:

1. Insufficient and delayed digestion of albuminoids *in vitro* by the filtrate of the gastric contents.

2. Protracted and augmented chloride secretion, especially of combined hydrochloric acid.

3. Abnormal amount of fermentation.

4. Retarded motility of the stomach.

5. Increase in activity of the pepsin of the gastric filtrate in artificial digestion by the addition of an extract of lamb's spleen.

6. Subjective phenomena on the part of the individual showing a certain gastric hyperexcitability with the paste of Ferrannini and a discrete diminution in the body weight.

From these data Gallenga concluded that:

1. The spleen most probably has an active part in the gastric digestion of albuminoids, as is proved to occur in pancreatic digestion.

2. This action of the spleen must depend on an internal secretion, pepsinogenic, which exerts an influence on the quantity of the juice poured out and the activity of the pepsin.

3. In persons splenectomized the peptonization of albuminoids in the stomach and *in vitro* with extracted gastric juice is markedly delayed and diminished, although in a certain degree compensated for by an augmented chloride secretion.

In 1903 Silvestri performed some animal experiments which led him to the conclusion that the digestive power and the quantity of the gastric juice are constantly augmented after splenectomy. He found that in the dog and cat immediately after removal of the spleen gastro-intestinal phenomena intervene, and that though appetite is conserved, weight is lost. When the animals were sacrificed after four days an enormous dilatation of the stomach was observed which Silvestri thought could not be blamed to operative trauma. To three dogs before and after splenectomy he administered a secretory meal of soup and meal and injected apomorphin after four, six and eight hours respectively in order to secure vomiting. He observed that the material vomited was in less quantity and in a more advanced state of digestion in the splenectomized dog. Later he fed animals a mixture of bread with 200 gm. of meat divided into small cubes, and after five hours opened the stomachs; they contained brownish liquid with pieces of meat more abundant and larger in the control animals than in the splenectomized animals. In artificial digestion with the non-filtrated gastric contents he found less peptic activity in splenectomized dogs, but on the contrary more activity after filtration of their chyme. This, he considered, proved that digestion was more advanced in those splenectomized. Again, using *in vitro* experiments with filtrated gastric contents, he found a hyperpepsia following removal of the spleen. Splenec-

tomized dogs had the capacity of transforming enormous quantities of albuminoids in their stomachs.

In a later communication he stated that:

1. An internal secretion of the spleen with trypsinogenic or pepsinogenic function cannot be demonstrated.

2. The spleen plays a mechanical part in digestion and can be considered as a regulator of the circulation of the abdominal digestive organs.

3. The infusions of spleen in the height of digestion most probably exert influence on pancreatic extracts and the gastric mucosa by virtue of their leukocyte content, since these cells, as has been shown by other workers, contain a ferment, kinase, with digestive powers.

Silvestri reported the case of a woman of thirty with syphilis who had a large spleen and was splenectomized. Four months later she aborted a two months' fetus, after which Silvestri took up the study of the patient's gastric motility and chemistry. He found the gastric motility intact while the digestive power was superior to normal.

Likewise Tini, in 1909, found an augmentation in the gastric secretion and peptic activity, concluding that there is an antagonism between the pancreas and the stomach in the mode of action exercised on them by the spleen, splenectomy decreasing the trypsin function of the pancreas and augmenting the pepsin activity of the stomach.

Betti, in 1909, reported observations on a dog with a gastric fistula. He used Mett's method of determining peptic activity and also introduced 10 gm. meat cubes into the stomach. These cubes lost from 2.8 gm. to 3 gm. in weight before splenectomy and only 0.6 gm. to 0.4 gm. after splenectomy. The dog became markedly voracious. The author explained the objection that splenectomized animals live and digest well by citing the fact that animals can also live without a stomach. His deductions were therefore (1) in splenectomized animals the digestive power is notably diminished and (2) the spleen intervenes in gastric digestion by sending a substance that can be considered, as much from its genesis as its action, analogous to the enterokinase of Pawlow, and with all probability it serves to activate the zymogen into active ferment. This would easily explain the observations of Baccelli that the spleen in malaria, sclerotic and inelastic from the process of chronic splenitis, receives much less blood than a spleen normal and elastic; as a result there is a notable diminution in kinase.

Gross, in 1910, reported the case of a young man who was splenectomized ten hours after rupture of the spleen due to a hoof-kick in the abdomen. After recovery he attended a reception at which he overate and was seized with abdominal cramps. This suggested to Gross the advisability of investigating the patient's digestive juices. The amount of trypsin in the duodenal contents and stools was normal. The peptic activity of the gastric juice was determined

after an Ewald meal by the method of pepsin determination introduced by Gross and now known by his name (precipitation of faintly alkaline solutions of casein by means of acetic acid; no precipitation on complete digestion). He found, four weeks after splenectomy, a marked decrease in the pepsin strength, which gradually rose almost to normal within three months and was completely normal at the end of seven months. At the same time he carried on studies of the blood and noted a relative lymphocytosis which disappeared gradually in ratio as the strength of the pepsin rose. From this he suggested an interrelation between the lymphocytosis and the decrease of peptic activity.

Trampedach, in 1911, carried on a careful and exhaustive series of researches:

In the first investigation he sought to simulate the method of Gross as nearly as possible; a dog was given a test breakfast, which was removed by the stomach-tube. Chyme was obtained which was not acid, a finding which the experimenters, in view of the newer observations on the distribution of the acidity of the stomach in layers, did not consider wonderful. Later a Pawlow cannula was inserted into the dog, the chyme obtained after a test breakfast and an analysis for its pepsin content made. The determinations were carried out with Mett's tubes filled with wether serum instead of egg albumen.

In the second investigation Trampedach attempted to avoid the incomplete emptying of the stomach, which might have happened in the first investigation. To this end a special cannula, 2 cm. in diameter, was inserted into the duodenum. By the introduction of rubber balloons, barriers were put up and removed at will in order to have all the experiments exactly alike. As test-meals, 100 gm. portions of sterilized flesh and 25 gm. portions of dried ground white bread were used. The chyme obtained was tested (1) for its content of dissolved nitrogen in the filtrate, and by this means the degree of digestion in the stomach determined; (2) it was put with equal parts of tenth normal hydrochloric acid and let stand to digest for twenty-four hours, the amount of peptic activity then being ascertained by the determination of the dissolved nitrogen in the filtrate; and (3) it was investigated for proteolytic power by means of Mett's tubes.

In the third investigation pieces of mucous membrane were cut from different places of a dog's stomach and the spleen extirpated at the same time. The infusions from the pieces of mucous membrane obtained were tested for pepsin activity after the method of Mett. When the animal had completely recovered from the interference it was killed and similar pieces of mucous membrane from corresponding parts of the stomach were tested for their pepsin content.

In the fourth investigation the spleens were extirpated in a number

of rats. After the animals had recovered from the operations a splenectomized rat and a control rat were killed, and the infusion of each stomach tested for its peptic power.

From these experiments Trampedach arrived at the conclusion that extirpation of the spleen has no diminishing influence on the digestive power of the stomach. He found no relation between the post-splenectomy lymphocytosis and the secretion of pepsin.

Rusca, in 1912, reported a case of splenomegalia malarica with torsion of the splenic pedicle and anemia. Splenectomy was performed; the anemia improved and ten days later gastric researches on the patient were made. By percussion and roentgenologically the stomach was found to be ptotic and the emptying time four hours. Ewald, Boas and Leube test-meals were used. An increase of free hydrochloric acid was found but not invariably, and a constant and marked diminution in the content of pepsin, more striking with the method of Gross than with that of Mett. After Leube's meal a diminution in the power of fragmentation and disintegration of meat fiber was quite in evidence microscopically. Gastric motor function was good.

Rusca produced cirrhosis of the spleen in a dog by injecting the pneumobacillus of Friedländer and found diminished peptic activity thereafter. He surmised that the sclerosis thus caused interfered with the gastrosplenic circulation described by Baccelli and so hindered the afflux of the hypothetical activating ferment to the stomach.

In two cases of leukemia and two of malaria Rusca determined the size of the spleen, the leukocyte count, the relative lymphocytosis, the gastric acidity, the gastric activity of digestion of meat fibers and the trypsin content of the feces, but he could reach no conclusions from his results as to the rôle of the spleen in digestion. One patient with leukemia showed a marked reduction of pepsin, whereas in the others the gastric digestion was normal. All, however, had hyperchlorhydria.

Rusca also studied in 1912 the gastric function in six dogs before and after splenectomy, using an Ewald test-meal of 50 gm. bread and 250 c.c. water, and extracting it with the stomach-tube three-quarters of an hour after ingestion. He found a slight diminution in pepsin after splenectomy and slight unimportant variations in the amount of total acids. He obtained evidence neither of digestion of starch nor of lipolytic activity. There was no free hydrochloric acid. The dogs had voracious appetites and gained weight. The diminution in peptic power he thought to be compensated for by the augmentation of appetite and the greater amount of aliment taken.

Rusca likewise observed that in a dog with a gastric fistula following splenectomy peptic activity decreased somewhat after meals of milk, meat and oil. In experiments on a bitch which had been

splenectomized about three months previously he found a marked persisting voracity and could not corroborate Gross's findings that the pepsin power returned to normal after several months.

He considered the question of the influence of the spleen on digestion not yet settled. In just what manner the spleen acts he thought it not possible to say; probably it has a purely vascular influence, forming a sort of receptacle for the blood which accumulates there in its ample lacunæ coincidently with the congestion of all the abdominal organs during digestion. The spleen then contracts and sends the blood through the peculiar gastrosplenic system to the peptic cells, offering there in greater quantity the necessary pabulum for the elaboration of pepsin.

Soler and Madero made an experimental communication in 1912 with regard to this subject. They used dogs with Pawlow stomach pouches. At first they had great difficulty in keeping the dogs alive; the animals lost 40 per cent. of their initial weight and died within from one to one and one-half months. After diets of milk and of meat an immediate and marked drop was found in the peptic power of the gastric secretion following removal of the spleen, while coincident and parallel with this the erythrocyte count diminished. Pepsin was measured by Mett's tubes, amylolytic ferment (?) by titration with Fehling's solution (after clearing with lead subacetate the sugar solution acted on), lipase by allowing 2 c.c. of juice to stand ten hours at 38° C. with 1 c.c. of olive oil, dissolving this then with 50 c.c. of alcohol and titrating with sodium hydroxide the amount of fatty acids developed. They noted a diminution of lipase after splenectomy, and concluded that there is a like diminution of gastric amylase if such exists. More lipase was secreted after a meal of milk than after one of meat. By computing the peptic activity in digestive units (obtained by multiplying the amount of secretion by the quantity of pepsin) they found a greater drop in the amount of pepsin after splenectomy than when this was measured directly by the number of millimeters of Mett's tubes digested. With both milk and meat secretory meals the digestive curve before splenectomy rose to the highest points the first and second hour and dropped fairly acutely to end in seven hours. After splenectomy the fall in the digestive curve was more gradual and did not reach normal for from nine to twelve hours. This they considered was because the digestive units were fewer and thus the juice would have to act longer to accomplish a given amount of digestion. Soler and Madero concluded: "We think, therefore, in view of the proof as we have offered it, that the spleen is an organ which evidently assists physiologically in the elaboration of the gastric ferments."

In 1915 Soler and Madero published a paper reviewing their former work and discussing it and their methods in detail. Furthermore, they gave the results of a series of injections with splenic

products, "hormonal," and decoctions and macerations of dog's spleen. Invariably they obtained an increase in peptic activity after such injections. Some of these experiments were performed on a dog splenectomized three years previously. This influence of splenic extract they determined was not due to the solution used for decocting and macerating spleens, for injected alone in greater amounts it had no effects. Next they studied the influence of the serum of the splenic vein as compared with that of the splenic artery and found it much superior in stimulating effect. They considered this distinctive action due to elements in the spleen, most probably to the leukocytes which exist in this organ in such enormous quantity. Later they used extracts of lymph glands, of the spleen, leukocytes and washed erythrocytes (which probably contained a large amount of leukocytic material) both of the dog and of the horse, with similar results. The mesenteric lymph glands alone gave negative findings in contrast to those mentioned, their excitosecretory function on the stomach being nil. They found after the injection of splenic products that the erythrocytes increased as much as the leukocytes.

In *resume*, Soler and Madero concluded that (1) splenectomy diminishes the digestive power of the stomach; (2) the injection of macerations and decoctions of the spleen whether obtained from the same or different species increases the digestive power of the stomach; (3) the splenectomized animals diminish in weight to reach a stationary level, but require double the amount of nutriment for sustenance; (4) the injection of splenic products provokes a frank augmentation of weight in the dogs splenectomized, but has little or no influence on those not splenectomized; and (5) the blood formula shows that in splenectomy the erythrocytes follow a curve parallel with that of the fermentative power, being inverse to that of the leukocytes, while following the injection of macerated material (splenic infusion) the augmentation of both occurs conjointly.

Experimental Methods.

In the present experimental study healthy female dogs weighing on the average about 10 kg. were used. Accessory stomachs or fundic sacs with blood and nerve supply intact and communicating with the outside were made according to a slightly modified Pawlow technic. Fifteen animals were prepared, on three of which only were complete data obtained before and after splenectomy. Most of the others succumbed to distemper, then epidemic in the laboratory, a few to the primary operation.

The dogs were placed in pillories and the juice collected by inserting into the pouches large fenestrated rubber tubes with wide funnel-shaped cuffs which were held snugly against the abdominal wall by an appropriate harness. The loss of juice in collection was negligible.

However, digestion of the skin about the openings of the miniature stomachs could not be prevented entirely although it was obviated as much as possible by the use of divers ointments, beds of sand or shavings, continuous drainage by leaving the tube in place at all times and so forth.

The animals were deprived of food on the evening previous to the experiment and of water one hour before the giving of the secretory meal, which consisted of raw meat cut into small cubes. The diet at other times was bread and milk. In some instances the amount of continuous gastric secretion was determined by collecting the juice for one hour previous to feeding. In all cases the dogs lost some weight after each operative procedure, but, on the whole, their state of nutrition remained good with the exception of those which developed distemper and of Dog. E.

The gastric juice was collected for six hours after feeding, the amount measured, the free and total acidity ascertained by titrating 1 c.c. of clear juice diluted with 25 c.c. of distilled water, with dimethylamidoazobenzol and phenolphthalein as indicators, and the pepsin activity determined by Mett's method. Fortieth normal sodium hydroxide was used for the titration, the acidity found being expressed in percentages of hydrochloric acid; and 1 c.c. of juice diluted with 5 c.c. of tenth normal hydrochloric acid placed with Mett's tubes (egg albumen coagulated just below boiling) at 39° C. for twenty-four hours for the digestive strength, the result being expressed directly in the number of millimeters of albumen digested (average of four readings). When a norm was established for the gastric secretion in each instance the spleen was removed under ether anesthesia preceded by an injection of one-fourth grain morphin and one one-hundred and fiftieth grain atropin. Determinations were again made on the gastric secretion as before, and at the conclusion of each experiment a necropsy was performed to rule out the presence of unremoved or accessory splenic tissue.

Experimental Data.

The protocols of experimental data are as follows:

PROTOCOL 1.—DOG D: NORMAL WITHOUT SPLENECTOMY. PAWLOW POUCH MADE APRIL 11, 1917. SECRETORY MEAL, 100 GM. MEAT.

Date, 1917.	Amount of juice for six hours. c.c.	Free acid.	Combined acid.	Total acidity.	Pepsin (Mett's tubes), mm.
April 16	18.2	0.09	0.11	0.20	3.70
17	24.6	0.24	0.09	0.33	3.05
18	9.7	0.08	0.08	0.16	3.05
19	15.8	0.09	0.09	0.18	3.05
20	14.3	0.04	0.08	0.12	4.30
Averages	16.5	0.11	0.09	0.20	3.43

Dog D remained in good condition until April 21 when symptoms of distemper appeared. The dog died from distemper April 28.

PROTOCOL 2.—DOG F: NORMAL WITHOUT SPLENECTOMY. PAWLOW POUCH MADE APRIL 19, 1917. SECRETORY MEAL, 150 GM. MEAT.

Date, 1917.	Amount of juice for six hours. c.c.	Free acid.	Combined acid.	Total acidity.	Pepsin (Mett's tubes), mm.
April 23	14.0	0.09	0.16	0.25	2.75
24	49.0	0.00	0.20	0.20	2.70
25	56.0	0.09	0.17	0.26	1.50
26	43.3	0.07	0.20	0.27	2.90
27	43.9	0.00	0.20	0.20	3.85
28	42.6	0.00	0.16	0.16	2.30
29	34.3	0.00	0.20	0.20	5.00
30	32.2	0.00	0.14	0.14	3.05
May 14	19.6	0.00	0.07	0.07	2.00
16	28.0	0.00	0.18	0.18	4.60
Average	37.3	0.25	0.168	0.193	3.065

Dog F remained in good condition until May 1 when it developed a mild distemper and lost weight markedly; it recovered May 13, and two more determinations were made. A marked inanition developed, however, and because of this and the extreme variability of the normal determinations the experiment was abandoned.

PROTOCOL 3.—DOG L: PAWLOW POUCH MADE JUNE 10 AND SPLENECTOMY PERFORMED AUGUST 1, 1917. SECRETORY MEAL, 150 GM. MEAT.

BEFORE SPLENECTOMY.

Date, 1917.	Amount of juice for six hours. c.c.	Free acid.	Combined acid.	Total acidity.	Pepsin (Mett's tubes), mm.
June 30	12.0	0.17	0.09	0.26	3.25
July 2	14.0	0.17	0.10	0.27	4.00
3	21.0	0.16	0.10	0.26	3.875
4	17.0	0.18	0.09	0.27	3.25
7	14.0	0.16	0.10	0.26	3.5
8	16.0	0.21	0.07	0.28	3.375
10	14.6	0.12	0.10	0.22	3.68
11	10.0	0.05	0.14	0.19	3.375
12	27.0	0.19	0.15	0.34	1.50
24	24.0	0.21	0.11	0.32	2.625
26	30.0	0.15	0.26	0.41	2.625
28	39.0	0.18	0.07	0.25	1.80

AFTER SPLENECTOMY.

Aug. 4	26.7	0.32	0.07	0.39	2.20
5	12.0	0.20	0.07	0.27	3.50
6	12.0	0.23	0.09	0.32	3.50
7	18.0	0.16	0.10	0.26	3.80
8	40.0	0.21	0.11	0.32	3.70
9	15.0	0.08	0.16	0.24	3.25
10	20.0	0.36	0.10	0.46	3.00
11	18.4	0.15	0.08	0.23	3.85
12	16.0	0.10	0.07	0.17	2.68
AVERAGE BEFORE SPLENECTOMY.					
	19.9	0.16	0.12	0.28	3.05
AVERAGE AFTER SPLENECTOMY.					
	14.9	0.20	0.095	0.295	3.25

Dog L remained in good condition throughout the experiment and at its conclusion was killed by etherization. No accessory splenic tissue was found at necropsy.

PROTOCOL 4.—DOG M: PAWLOW POUCH MADE JUNE 17. SPLENECTOMY PERFORMED JULY 31, 1917. SECRETORY MEAL, 150 GM. MEAT.

Date, 1917.	Amount of juice for six hours. c.c.	Free acid.	Combined acid.	Total acidity.	Pepsin (Mett's tubes), mm.
Before Splenectomy.					
July 4	15.0	0.34	0.09	0.43	4.0
6	18.0	0.29	0.10	0.39	4.1
7	19.0	0.15	0.16	0.31	4.5
8	20.0	0.21	0.13	0.34	2.6
9	19.7	0.14	0.17	0.31	2.04
10	24.0	0.17	0.21	0.38	3.16
11	34.0	0.35	0.10	0.45	3.75
12	25.0	0.10	0.13	0.33	3.00
24	15.0	0.15	0.29	0.44	3.50
26	18.0	0.13	0.26	0.39	3.00
28	30.4	0.23	0.16	0.39	3.85
29	20.0	0.36	0.11	0.47	2.875
30	25.0	0.27	0.11	0.38	2.69
After Splenectomy.					
Aug. 4	14.4	0.16	0.15	0.31	2.40
5	13.0	0.20	0.15	0.35	3.50
6	16.0	0.21	0.11	0.32	3.60
7	23.0	0.25	0.16	0.41	3.60
8	19.0	0.23	0.15	0.38	3.44
9	30.0	0.29	0.12	0.41	3.50
10	17.0	0.15	0.22	0.37	4.00
11	19.2	0.13	0.11	0.24	2.90
12	17.0	0.14	0.15	0.29	3.30
Average before Splenectomy.					
	21.8	0.22	0.16	0.38	3.31
Average after Splenectomy.					
	18.7	0.20	0.15	0.35	3.31

Dog M remained in good condition throughout the experiment and at its conclusion was killed by etherization. No accessory splenic tissue was found at necropsy.

TABLE 1.—DOG L: HOURLY DETERMINATIONS BEFORE AND AFTER SPLENECTOMY.

Date. July 9, 1917.	Pepsin (Mett's tubes), mm.	Amount of juice, c.c.	Free acid.	Combined acid.	Total acidity.
Before Splenectomy.					
First hour	5.00	4.20	0.11	0.09	0.20
Second hour	4.75	3.80	0.20	0.06	0.26
Third hour	3.75	3.20	0.18	0.07	0.25
Fourth hour	3.00	3.00	0.18	0.05	0.23
Fifth hour	2.90	2.00	0.12	0.04	0.16
Sixth hour	2.50	2.20	0.07	0.21	0.26
After Splenectomy.					
August 2, 1917.					
First hour	3.25	3.20	0.14	0.06	0.20
Second hour	2.50	3.60	0.13	0.07	0.20
Third hour	2.25	2.00	0.10	0.07	0.17
Fourth hour	2.25	2.60	0.06	0.08	0.14
Fifth hour	2.31	2.40	0.09	0.06	0.15
Sixth hour	3.44	2.20	0.06	0.07	0.13

PROTOCOL 5.—DOG E: HEIDENHAIN POUCH MADE APRIL 13. SPLENECTOMY PERFORMED APRIL 26, 1917, AT 9 P.M. SECRETORY MEAL, 100 GM. MEAT.

Date.	Hour preceding feeding.	Amount collected each hour.						Amount of mucus.	Pure juice.	Total amount collected	Free acid.	Combined acid.	Total acidity.	Pepsin (Mett's tubes).
		First.	Second.	Third.	Fourth.	Fifth.	Sixth.							
1917.					BEFORE SPLENECTOMY.									
		C.c.	C.c.	C.c.	C.c.	C.c.	C.c.	C.c.	C.c.	C.c.				
April 18	2.8	11.4	11.0	12.0	14.8	9.4	7.2	3.8	62.0	65.8	0.32	0.10	0.42	2.00
19	...	6.2	5.0	7.6	8.4	11.0	9.2	1.8	45.6	47.4	0.36	0.07	0.43	2.10
20	2.6	6.8	7.2	10.0	9.2	6.5	3.7	...	...	45.4	0.34	0.09	0.43	1.88
21	3.5	9.8	5.2	10.6	12.7	9.6	5.1	2.4	50.6	53.0	0.32	0.10	0.42	2.10
22	1.8	11.2	15.2	13.0	7.0	4.4	3.2	0.8	52.3	54.0	0.41	0.06	0.47	1.92
23	1.2	9.0	17.8	20.8	11.3	13.7	12.0	1.6	83.1	84.7	0.41	0.06	0.47	1.95
24	2.4	11.2	7.0	5.4	8.0	7.6	7.0	0.8	45.4	46.2	0.40	0.05	0.45	2.14
25	1.0	5.9	5.6	5.4	7.4	6.8	6.5	0.8	36.2	37.0	0.37	0.08	0.45	1.83
26	1.2	10.2	13.6	17.6	13.6	12.8	9.4	0.6	76.6	77.2	0.46	0.04	0.50	1.81
					AFTER SPLENECTOMY.									
April 27	...	7.0	4.0	7.0	3.8	2.8	2.5	1.4	25.7	27.1	0.36	0.09	0.45	1.56
28	0.7	8.0	9.4	8.7	5.2	5.0	5.4	3.0	38.7	41.7	0.40	0.05	0.45	1.50
29	0.8	10.2	6.8	6.4	7.8	5.6	6.6	0.6	42.8	43.4	0.43	0.04	0.47	1.74
30	3.4	15.2	22.0	21.6	14.2	11.2	12.0	0.8	95.4	96.2	0.46	0.04	0.50	1.87
May 1	2.8	6.2	11.6	12.8	6.2	3.8	2.6	2.2	41.6	43.8	0.34	0.08	0.42	2.10
2	1.6	10.0	10.2	8.0	9.2	6.8	4.0	2.4	45.8	48.0	0.33	0.09	0.42	2.00
3	2.4	11.8	9.4	12.8	12.6	6.6	5.6	2.2	56.6	58.8	0.39	0.07	0.46	2.00
4	...	5.6	7.2	7.3	7.6	7.2	6.2	2.4	38.7	41.1	0.33	0.05	0.38	2.00
5	...	5.2	5.2	6.8	6.2	6.0	4.8	1.4	32.8	34.2	0.30	0.60	0.36	1.85
					AVERAGE BEFORE SPLENECTOMY.									
	2.08	9.1	9.7	11.6	10.3	9.1	7.0	1.6	56.6	57.0	0.38	0.07	0.45	1.97
					AVERAGE AFTER SPLENECTOMY; FIRST TWO DAYS OMITTED.									
	2.5	9.2	10.3	10.8	9.2	7.0	6.0	1.5	50.5	52.2	0.37	0.06	0.43	1.94

Dog E began losing weight immediately after the operation and lost steadily and progressively until its death, May 9. No other abnormal findings, save the development of bloody stools the last forty-eight hours of life, were noted. At necropsy the isthmus connecting the pouch to the main stomach was very small, making it probable that the vagus fibers to the pouch were partially, if not totally, severed at the time of the first operation. There was no accessory splenic tissue. No cause for death could be found.

TABLE 2.—DOG M: HOURLY DETERMINATIONS BEFORE AND AFTER SPLENECTOMY.

BEFORE SPLENECTOMY.

	Pepsin (Mett's tubes).			Amount of juice.			Free acid.			Combined acid.			Total acidity.		
	July 9, 1917.	July 28, 1917.	Average.	July 9, 1917.	July 28, 1917.	Average.	July 9, 1917.	July 28, 1917.	Average.	July 9, 1917.	July 28, 1917.	Average.	July 9, 1917.	July 28, 1917.	Average.
	Mm.	Mm.	Mm.	C.c.	C.c.	C.c.									
First hour	2.80	4.30	3.55	3.0	9.0	6.1	0.17	0.22	0.195	0.17	0.14	0.155	0.34	0.36	0.35
Second hour	1.50	3.60	2.55	3.3	6.8	5.05	0.17	0.30	0.235	0.21	0.16	0.185	0.38	0.46	0.42
Third hour	1.87	3.50	2.685	2.6	4.0	3.3	0.14	0.26	0.20	0.17	0.15	0.16	0.31	0.41	0.36
Fourth hour	1.70	3.50	2.60	3.6	4.0	3.8	0.16	0.25	0.205	0.20	0.16	0.18	0.36	0.41	0.385
Fifth hour	2.56	4.00	3.28	3.2	3.4	3.3	0.15	0.19	0.17	0.18	0.17	0.175	0.33	0.36	0.345
Sixth hour	2.61	3.80	3.205	2.4	3.0	2.7	0.16	0.09	0.125	0.18	0.19	0.185	0.34	0.28	0.31

AFTER SPLENECTOMY.

	Aug. 11, 1917.	Aug. 12, 1917.	Average.	Aug. 11, 1917.	Aug. 12, 1917.	Average.	Aug. 11, 1917.	Aug. 12, 1917.	Average.	Aug. 11, 1917.	Aug. 12, 1917.	Average.	Aug. 11, 1917.	Aug. 12, 1917.	Average.
First hour	4.00	4.75	4.375	2.2	3.6	2.9	0.00	0.08	0.04	0.12	0.17	0.145	0.12	0.25	0.185
Second hour	4.35	3.19	3.77	3.0	3.6	3.3	0.04	0.20	0.12	0.21	0.15	0.18	0.25	0.35	0.30
Third hour	3.55	2.75	3.15	4.2	2.2	3.2	0.11	0.16	0.135	0.16	0.16	0.16	0.27	0.32	0.295
Fourth hour	2.34	2.60	2.47	3.0	2.8	2.9	0.12	0.14	0.13	0.17	0.12	0.145	0.29	0.26	0.275
Fifth hour	2.65	2.44	2.545	3.8	2.6	3.2	0.09	0.15	0.12	0.20	0.11	0.155	0.29	0.26	0.275
Sixth hour	3.27	3.60	3.435	3.0	2.2	2.6	0.07	0.11	0.09	0.21	0.16	0.185	0.28	0.27	0.275

TABLE 3.—DOG E: HOURLY DETERMINATIONS BEFORE AND AFTER SPLENECTOMY.

BEFORE SPLENECTOMY.

	Pepsin (Mett's tubes).			Free acid.			Combined acid.			Total acidity.		
	Mar. 24, 1917.	Mar. 25, 1917.	Average.	Mar. 24, 1917.	Mar. 25, 1917.	Average.	Mar. 24, 1917.	Mar. 25, 1917.	Average.	Mar. 24, 1917.	Mar. 25, 1917.	Average.
	Mm.	Mm.	Mm.									
First hour	1.80	2.70	2.25	0.40	0.32	0.36	0.06	0.04	0.05	0.46	0.36	0.41
Second hour	1.35	2.05	1.70	0.44	0.36	0.40	0.04	0.04	0.04	0.48	0.40	0.44
Third hour	1.65	1.70	1.695	0.39	0.36	0.375	0.05	0.04	0.044	0.44	0.40	0.42
Fourth hour	2.00	1.70	1.85	0.39	0.39	0.39	0.05	0.05	0.05	0.44	0.44	0.44
Fifth hour	1.75	1.40	1.575	0.41	0.38	0.405	0.05	0.06	0.055	0.46	0.44	0.45
Sixth hour	1.65	1.40	1.525	0.39	0.38	0.385	0.06	0.07	0.65	0.45	0.45	0.45

AFTER SPLENECTOMY.

	Mar. 28, 1917.	Mar. 30, 1917.	Average.	Mar. 28, 1917.	Mar. 30, 1917.	Average.	Mar. 28, 1917.	Mar. 30, 1917.	Average.	Mar. 28, 1917.	Mar. 30, 1917.	Average.
First hour	2.80	2.00	2.40	0.43	0.39	0.41	0.04	0.08	0.06	0.47	0.47	0.47
Second hour	1.90	1.30	1.60	0.48	0.41	0.445	0.04	0.07	0.055	0.52	0.48	0.50
Third hour	1.45	1.50	1.475	0.48	0.40	0.44	0.04	0.07	0.055	0.52	0.47	0.495
Fourth hour	1.95	1.45	1.70	0.46	0.38	0.42	0.05	0.07	0.06	0.51	0.45	0.48
Fifth hour	1.75	1.15	1.45	0.46	0.34	0.40	0.04	0.09	0.065	0.50	0.43	0.465
Sixth hour	1.40	1.60	1.50	0.44	0.34	0.39	0.05	0.06	0.055	0.49	0.40	0.0445

The peptic strengths and acidities in Protocol 5 corresponding to those of the four days in Table 3 were obtained by multiplying; for example, each hourly strength of pepsin by the amount of juice collected the corresponding hour, these added, and the total divided by the total amount of juice collected that day.

Review of Experimental Data.

Our experimental data show that splenectomy had apparently little influence on gastric secretion.

Protocols 1 and 2 illustrate the normal findings of gastric secretion under the conditions of this study and serve as controls for the splenectomized animals of Protocols 3 and 4. From the first four protocols it is seen that normally an amount of pepsin is secreted sufficient to digest approximately 3 mm. of egg albumen (Mett's tubes) in twenty-four hours. Ordinarily the peptic activity as illustrated in Protocols 2, 3 and 4 is quite constant and fluctuates little from day to day; the inconstancy shown in Protocol 2 is exceptional and the most marked that we have observed. The daily variation, however, in the proteolytic power of the juice in the cases of Dog L and Dog M was less marked after splenectomy. It is doubtful whether any significance can be attached to this.

In Protocol 4 the total acidity is about that generally cited as normal, whereas Protocols 1, 2 and 3 show a subnormal acidity, approximately 0.2 per cent. The total acidity in each instance is likewise fairly consistent in amount, but not so consistent as the pepsin. On the other hand the amounts of free and combined acid fluctuate widely, in such manner, however, as to be mutually complementary. Hence changes in the relative proportions of these acidities after extirpation of the spleen mean little. It is interesting to note that Dog F showed the presence of free acid on a few occasions only.

In the quantity of secretion obtained in six hours the important determining factors are the size of the Pawlow pouch and the amount of the secretory meal. In the experiments under discussion about 25 c.c. for each 150 gm. of meat given were secreted by the miniature stomach. This is rather a low rate, but the pouch in each instance was small. The daily variation in the quantity of juice was quite marked, depending probably to a large extent on psychic and other extrinsic factors influencing the stomach through its secretory and motor nerves. Because of this variability slight changes following any experimental procedure cannot be given the weight otherwise to be accredited them.

In Protocols 3 and 4 the only noteworthy result following splenectomy was a diminution in the quantity of secretion, 25 per cent. decrease in Dog. L and 14 per cent. in Dog M (Fig. 1). This might possibly have been due to the interference with, and resulting decrease of, the gastric blood supply consequent on the operation, especially the injury to the gastrosplenic circulation through the vasa brevia. The determinations in each case were made too soon after the removal of the spleen for the post-splenectomy anemia to play a causative role.

The data given in Protocol 5 are considered separately, for, as was

found at necropsy, we were dealing with an accessory stomach of the Heidenhain type rather than of that of Pawlow as we thought. This lack of nervous control over the pouch gave noteworthy differences from the normal secretory findings: (1) With a secretory meal of only 100 gm. of meat, the amount of juice obtained in six hours, 50 c.c., was twice that of the other dogs with a meal of 150 gm.; (2) the daily fluctuation in amount of juice was less; (3) the free acidity was persistently and consistently high, approximately 0.4 per cent.; and (4) the strength of pepsin was low (2 mm.) but quite constant. This daily non-variability of the quantity of juice secreted, of the acidities, and of the proteolytic power would be expected from severance of the pouch from extrinsic influences through the nervous system. Since no cause for death could be

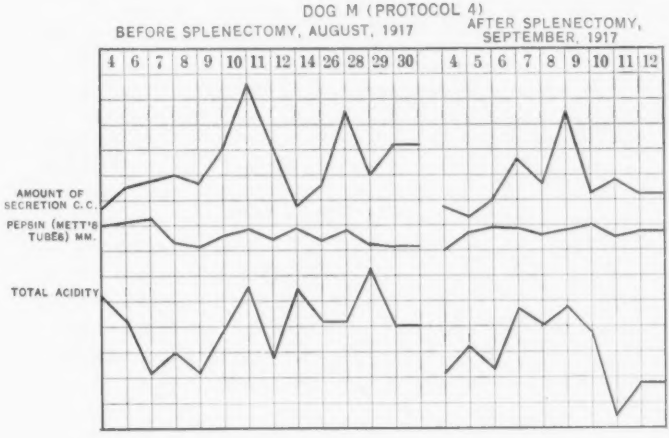
DOG M (PROTOCOL 4)
BEFORE SPLENECTOMY, AUGUST, 1917
AFTER SPLENECTOMY, SEPTEMBER, 1917
4 6 7 8 9 10 11 12 14 26 28 29 30
4 5 6 7 8 9 10 11 12
AMOUNT OF SECRETION C.C.
PEPSIN (METT'S TUBES) MM.
TOTAL ACIDITY

FIG. 1

found in this dog the idea suggests itself that possibly the loss of large quantities of juice from daily secretory meals, especially the loss of such great quantities of acid as occurred in this case, may have set up metabolic and acid-base-equilibrium disturbances sufficient to cause death.

Dog E of this experiment was splenectomized at 9 in the evening after it had had a secretory meal the same day, and was given a similar feeding the next morning, with the express purpose of seeing the immediate effect of splenectomy. After operation the pepsin strength was reduced, gradually rising to regain its normal about the third or fourth day. However, it seems logical to attribute this fall in proteolytic activity to the effect of the operation—anesthetic with following nausea and decrease in appetite, shock resulting from the operative trauma with the reaction on all the

body processes, and the effect of the atropin, given just before the operation, in checking gastric secretion. Hence it seems justifiable to omit from the general averages in this protocol the first two days after splenectomy, allowing this amount of time for recovery from the operation.

This experiment likewise shows no marked change in gastric secretion following splenectomy, though it is again noted that there is a decrease (8.5 per cent.) in the amount of juice obtained.

Tables 1, 2 and 3, and a portion of Protocol 5, give hourly determinations of gastric juice before and after splenectomy (Fig. 2). The average continuous secretion of juice from the pouch with the animal fasting was about 2 c.c. each hour in Dog E and much less than this in the other animals (figures not given). The amount of

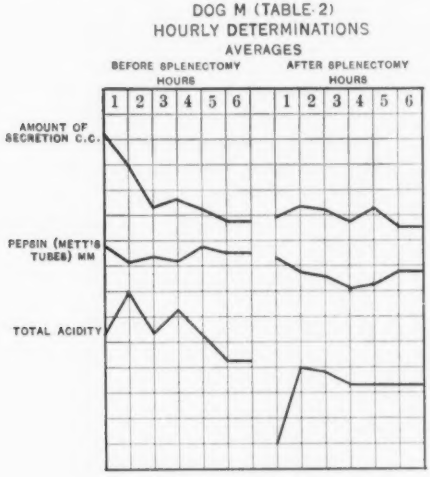

FIG. 2

juice secreted each hour varied through wide limits. With the Heidenhain pouch it rose gradually to reach a maximum the third hour and then diminished; with the Pawlow pouch the maximum occurred at any of the first three hours, most frequently at the first.

The pepsin content in nearly all instances was greatest the first hour, then dropped to show frequently a later secondary slight rise. The free acid and total acidity, it will be noted, reached a maximum from the second to the third hour only to fall again, whereas the combined acid remained about constant. These results (save the amount of juice secreted each hour in Dog E, which corresponds more to the normal of an intact pouch on a milk diet) coincide with those given by Pawlow as the normal hourly variation in gastric secretion in dogs on a meat diet.

Our protocols show that after splenectomy there is no noteworthy change in the hourly variations of gastric secretion after a secretory meal.

Discussion.

As is true of almost every field of research on the spleen it is apparent that the experimental results of different investigators with regard to the relation of this gland to gastric secretion are widely different. Just where the reasons lie for this it is difficult to determine.

The methods used in the investigations of some of the workers are possibly open to criticism. It is well recognized that collection of gastric juice for analysis from a gastric fistula is not so satisfactory as from the Pawlow stomach, since the former admits of contamination with saliva and duodenal contents, and the secretory meal is not separated from the juice tested; in fact, almost any results can be obtained with a gastric fistula. Cubes of coagulated albumin for pepsin determination offer less accuracy than the Mett method, though the latter is not ideal; the surface of albumin exposed to the action of the pepsin is more variable and less easily controlled and the handling and weighing of the cubes fraught with possibilities of error. The data obtained clinically on splenectomized persons are of inconclusive value irrespective of results, since there is always present some disease process rendering splenectomy advisable which may enter into consideration, and, further, the unreliability of determinations of gastric secretions obtained through stomach tubes is notorious. Likewise in animals analyses of stomach contents obtained after a test-meal by means of the tube or by vomiting induced by apomorphin are to be questioned. Furthermore, some of the experiments were made without comparative control determinations before splenectomy, for example those of Gallenga and Gross, and the clinical researches of Silvestri and Rusca. In other instances insufficient experimental data were offered on which to base conclusions, for example Betti, who gave a few results obtained from only one dog.

The most recent researches, those of Soler and Madero, were carried on practically under the same experimental conditions as the present study, yet with greatly different results. In their papers they make no reference to preceding work and are alone in their maintenance of the theory that the spleen assists in the physiologic elaboration of several gastric ferments, pepsin, gastric lipase and gastric amylase (?) Their results with injections of splenic products, leukocytes, lymph glands and so forth are interesting and find support, so far as splenic extracts are concerned, in the observations of Tarulli and Pascucci.

The work of Trampedach is the most thorough, painstaking and exhaustive that has been done. His investigation like the present

study, does not demonstrate any change in gastric secretion following splenectomy.

These findings are further corroborated by the general experience of clinicians that splenectomy in man has no obvious effect on gastric digestion. However, since pepsin normally is furnished in excess of the amount absolutely needed a slight diminution following removal of the spleen need not necessarily cause gastric symptoms (for example the absence of complaint in many cases of achylia), and hence clinical observations in themselves mean but little.

It does not follow that although the spleen has no pepsinogenic function it may not have some other relation to the stomach. Only further researches can elucidate this point. It seems likely, however, that at least the gastrosplenic circulation through the vasa brevia is of some significance, whether merely mechanically cannot be said. The hematemeses of the splenomegalies, especially those of splenic anemia, have been explained on the basis of gastric varices and obstruction to the gastrosplenic circulation, and from a clinical standpoint suggest at least a pathologic splenic-gastric interrelationship.

From a critical review of the literature and my experiments I am led to believe that the spleen does not exert any influence on gastric secretion except possibly in a circulatory manner suggested by finding a slight diminution in the amount of secretion following splenectomy.

Summary.

The spleen and the stomach from the earliest times have been supposed to possess some close interrelationship. Baccelli, in 1868, demonstrated a gastrosplenic circulation through the vasa brevia, and first put forward the theory that the spleen plays a role in the elaboration of pepsin. Subsequent studies of this question have been made on dogs by testing gastric secretion before and after splenectomy. This has been done by the use of gastric fistulas and Pawlow pouches and by the removal of secretory meals through the stomach-tube. Similar studies on humans have been made by gastric analyses after splenectomy for various reasons. The results of these experiments have been contradictory. They may be summarized as follows:

1. Removal of the spleen causes a diminution of the proteolytic power of the gastric juice (Tarulli and Pascucci, Gallenga, Betti, Gross, Rusca, Soler and Madero).

2. Injection of splenic extracts (Tarulli and Pascucci, Soler and Madero) and of leukocytes and of extracts of lymph glands (Soler and Madero) increase the proteolytic power of the gastric juice of splenectomized animals.

3. Removal of the spleen causes an augmentation of the proteolytic power of the gastric juice (Silvestri, Tini).

4. Removal of the spleen has no effect whatsoever on gastric secretion (Trampedach).

The chief theory put forward by the first group of investigators has been that the spleen gives to the blood stream during digestion a substance which activates or leads to the further elaboration of the gastric enzymes, especially pepsin.

In this experimental study I have reported data concerning the gastric secretion findings before and after splenectomy on three dogs with accessory stomach pouches (secretory meal of meat) and on two similar dogs serving as controls. Removal of the spleen in these experiments caused no noteworthy changes in gastric secretion except a slight diminution in the quantity of gastric juice obtained.

I am led to conclude from my experimental inquiries and a critical review of the literature that a definite pepsinogenic function of the spleen has not been demonstrated and that the relation of the spleen to gastric secretion is probably merely vascular, the diminution in the amount of juice secreted after splenectomy being attributable to decreased gastric blood supply from injury to the gastrosplenic circulation.

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EVENTRATION OF THE DIAPHRAGM, WITH REPORT OF A CASE.[1]

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Among the rare lesions of the diaphragm is the condition originally described by Petit in 1790 and termed by him eventration. This term, though generally used, is a misnomer because no abnormal opening of the diaphragm exists. Such an opening constitutes a hernia diaphragmatica vera when the projecting abdominal viscera are covered with peritoneum or a hernia diaphragmatica spuria when no peritoneal covering exists. In eventration there is simply a thinning or relaxation of the diaphragm, the layers remaining intact and the structure assuming an elevated or higher position than normal. Isolated writers have preferred such terms as these: "high position," "elevation," "dilatation," "relaxation" and "congenital insufficiency." Bayne-Jones, in 1916, collected the reported cases to that time and reported one of his own, making 45 in all. Since that time we have been able to find reports of 2 more. These cases with the one we report make a total of 48 cases on record at the present writing.

With regard to the etiology the weight of evidence would seem to favor a congenital origin. Some of the arguments advanced are (1) its occurrence in the fetus and the newborn, (2) its association with other congenital anomalies, (3) the involvement of the left side in almost all cases, which coincides with the complexity of the development of the left diaphragm, and (4) the absence of compression of the lung and contiguous structures.

[1] Presented in abstract before the Association of American Physicians, Atlantic City, May 4, 1920.

Considered as an acquired lesion it has been supposed to follow disease of the muscle or of the nerves, and as a result of greatly increased abdominal pressure. Among the latter conditions pregnancy, ascites and megalocolon are important in producing increased pressure. However, as Bayne-Jones points out, "If this factor of increased pressure in the abdomen bore an important etiologic relationship to eventration the frequency of pregnancy in general and oftentimes in the same individual should find a counterpart in a large number of women suffering from eventration of the diaphragm." As a matter of fact the lesion is uncommon in women. Among 45 collected cases there were 36 males and 9 females.

The high position of the diaphragm due to the contraction of pulmonary fibrosis and adhesive pleuritis is a different lesion from that under consideration and will be discussed under diagnosis.

The clinical notes of our case are briefly as follows:

E. N., white, female, married, aged thirty-nine years, was admitted to the Jefferson Hospital on December 4, 1919, complaining of pain in the epigastrium and in the back with attacks of vomiting.

Family History. Negative.

Past Personal History. Negative, except for the usual diseases of childhood. She states that she has always been in good health until the present trouble. No pregnancies.

History of Present Illness. In September, 1919, that is about three months prior to coming under observation, she began to have pain in the epigastrium and left lower chest associated with attacks of vomiting. The pain radiated to the back. The pains have continued, with varying intensity, until the present time. At times they seem to bear some relation to the taking of food, but the relationship is not constant. Shortly after the onset the patient noticed that she became easily short of breath on exertion and was losing weight. The physician who saw her at the beginning of her illness made a diagnosis of gastric neurosis and a roentgen ray at that time aided in the elimination of gastric ulcer or cancer.

Physical Examination. This revealed the following: A fairly well-nourished adult female, no jaundice, eyes, mouth, ears and neck normal. Chest: Well formed and symmetric; expansion definitely limited on the left side, especially over the lower portion. Apex-beat not visible or palpable. Percussion revealed tympany below the third rib in the anterior axillary line, merging with the tympany over the stomach below. Posteriorly on the same side the percussion note below the middle of the scapula was high pitched and resembled the so-called flat tympany. The percussion note of the rest of the chest was clear and resonant. Breath sounds were everywhere normal except over the area of the altered percussion note on the left lower chest, where they were practically absent. During the auscultation of this area a sound suggesting

a splash was heard when the patient was moved. No coin sound could be elicited. The physical signs elicited suggested the possibility of a hydropneumothorax, and this was our provisional diagnosis when the patient was admitted to the hospital.

Blood: Examination revealed the following: Hemoglobin, 88 per cent.; red blood cells, 4,700,000; white blood cells, 9600; differential white cell count; large mononuclears, 8 per cent.; small mononuclears, 19 per cent.; polynuclears, 69 per cent.; eosinophils, 4 per cent.

Urine: Examinations were repeatedly negative.

A paracentesis of the left chest in the sixth interspace in the midaxillary line was negative. The fluoroscopic and stereoscopic *x*-ray examination revealed the following:

The left diaphragm was found considerably higher than the right and does not move on forced inspiration. The dome-shape is retained and no adhesions are evident at the costophrenic angle. The diaphragm has the appearance of an eventration, the cause of which is not apparent. There is just a suggestion of a slight amount of infiltration at the left apex. The barium meal in the stomach shows the cardiac end of the stomach in its proper relation to the left diaphragm, but because of the enormous distention of the colon with gas we are unable to determine whether the stomach is normal or not. We believe that the position of the diaphragm is not due to the gas in the colon.

As we were preparing this paper for presentation before this Association we came across another case of high position of the diaphragm in a baby, a few days old, who was referred for a roentgen-ray examination for a fractured arm. The left diaphragm was at the level of the second interspace. The heart was not displaced. There was no question of any abdominal trouble and there were no symptoms of any kind suggesting trouble either above or below the diaphragm. This case would seem to emphasize the congenital origin.

Discussion. In the past most of the diagnoses were made at postmortem or operation. The symptomatology and physical examination suggested a variety of lesions. In one group the symptoms were referable to the chest and pneumothorax, pneumohydrothorax, pulmonary fibrosis, chronic adhesive pleuritis with elevation of the diaphragm, etc., were diagnosed.

In another group gastro-intestinal symptoms predominated and the patient was considered as having a gastric lesion, a diaphragmatic hernia, etc. With the advent of the roentgen ray many of the difficulties in the differential diagnosis of these lesions were cleared up. The case of Sailer and Rhein[2] illustrates well this point. Their patient was considered as having at various times either a

[2] Am. Jour. Med. Sc., 1905, cxxix, 688.

pneumothorax, diaphragmatic hernia, pulmonary cavity or an elevated diaphragm. The roentgen ray was taken immediately after death and not developed until after autopsy, but the study of the plates showed that the diagnosis could have been readily made by this method.

The roentgen ray made the diagnosis in our case. In a number of physical examinations made after the roentgen ray had established the diagnosis we came to the conclusion that we could have been put on the right track if we had paid more attention to the inspection and palpation of the costal margin movements as pointed out in recent years by Hoover. There was a distinct widening of the subcostal angle on inspiration. The widening seemed to be due principally to a divergence of the left costal border. Several physicians who saw the patient with me at different times were able to verify this observation. The high position of the diaphragm placed it at a mechanical disadvantage in its function as an antagonist to the intercostal muscles. Low position of the diaphragm occurs in many of the conditions confused with eventration, such as pneumothorax, hydropneumothorax, etc., and, as a result of which, narrowing of the subcostal angle occurs. In certain forms of obsolete pleurisy with adhesions to the diaphragm and the chest wall and the diaphragm and lung there is likewise narrowing, according to Hoover, because under these conditions it has acquired a mechanical advantage in its traction to the costal border by reason of the adhesions which, acting as points of fixation, give approximately a straight line to the phrenic muscular strands from the central tendon to the left sternocostal region.

Among the reported cases the left half of the diaphragm is noted as being involved in all forty-six instances excepting three. The dome is usually regular in outline in contradistinction to that which is seen in the elevated diaphragm of adhesive pleuritis. As the structure is thinned its outline on the fluoroscope screen is less distinct than the normal diaphragm shadow. The lung on the affected side is often hypoplastic. The heart is oftentimes normally placed, although it may be found displaced in either direction in involvement of the same half of the diaphragm.

One of the arguments adduced in favor of the congenital origin of this lesion as against an acquired elevation due to the traction of adhesions is the external symmetry which the chest presents on inspection. This is in striking agreement with the observations which Ellis[3] noted in his report of a case of congenital absence of the lung. This same writer collected eighteen instances of what appeared to be certain examples of the condition. In all of them the chest was externally symmetrical, the opposite lung, heart,

[3] Am. Jour. Med. Sc., 1917, cliv, 33.

fluid or abdominal organs taking the place of the missing organ. If this is true in pulmonary aplasia it is likewise true in eventration with pulmonary hypoplasia, and is one of the strongest arguments against an acquired origin of the disease. In acquired lesions elevating the diaphragm to the extent seen in congenital eventration there is obvious flattening of the chest wall. The lung is the seat of obvious and demonstrable disease and the roentgen ray shows many and dense shadows. The lung above the diaphragm in eventration is normal unless there be some intercurrent pulmonary disease, such as pneumonia, which, however, has no etiologic relationship to the diaphragmatic condition. The inspection of the chest reveals nothing of note as far as symmetry is concerned. In cases of eventration associated with aplasia of the lung on the affected side the opposite lung may be enlarged sufficiently to extend over and furnish sufficient pulmonary tissue to give physical signs on the side of the absent organ. Even in hypoplasia the opposite lung may extend over to the hypoplastic side. Clinically it is not possible to demonstrate such overlapping. Even with the roentgen ray considerable difficulty may be encountered unless the shadows of the bronchial tree are clear and suggest a different distribution than normal.

THE RELATIVE VALUE OF LABORATORY AND CLINICAL METHODS OF STUDY IN THE DIAGNOSIS OF TUBERCULOSIS.[1]

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During the past three or four decades medicine has undergone a greater development than in all preceding centuries. The fact that we have lived during that time and been a part of that development makes it difficult for us to view this progress in its proper perspective, so we must leave the final estimate of this era to future generations. We may, however, not without profit stop and consider some of the general trends of this age and see where we have gone and where we are going.

This era has been marked by several particular characteristics, among which may be mentioned: (1) The development of bacteriology with the light which it has shed upon the causative factors of many diseases; (2) the intensive study of pathologic anatomy, familiarizing the physician with the macroscopic and microscopic

[1] Read before the Medical Society of the District of Columbia, Washington, D. C., October 20, 1920.

characteristics of the tissues as affected by disease processes, at first in the dead, and later in the living as found at operation; (3) the development of biochemistry with its revelations as to the reactions which take place within the body; (4) the development of the necessary technic to solve the problems in the various fields of laboratory research; (5) a gradual dependence upon laboratory and mechanic measures in study in preference to clinical observation; (6) the gradual development of specialties for the intensive study of subjects, diseases and methods.

We have now arrived at a stage of development where we can be proud of our profession and its achievements. While medicine is still far from being an exact science, we have eliminated much of the inexactness and have located some of that which remains. It is still well for us, however, to pause and see if we are working to the best advantage and developing in that manner which will be most productive of advancement for the future.

Sir James MacKenzie, that great teacher of modern medicine, possessed of a keen imagination and endowed with a broad vision, has pointed out many of the errors to which medicine has committed itself and has endeavored to direct present and future investigation into channels which will make it broader, more practical and more efficient.

The laboratory age will probably always stand out as the golden age in medicine. It is impossible for use to conceive of another like period of time in which so many truths could be revealed as in the period through which we are now passing. To be sure progress will continue and present knowledge will be elaborated and made more accurate and more practical. Such an era of progress through which we are now passing forces many hardships upon those who must keep pace with the advancements. With the truths which have been enunciated there have also been many half-truths and much error, all of which must be segregated and properly evaluated. This is a task which now lies before us.

With the preponderance of laboratory study has naturally come the revelation of a preponderance of laboratory facts, and these have absolutely dominated the medical mind. Things outside of the laboratory have been minimized and considered less worthy of study. Even the application of the ascertained facts in the clinic has been looked upon as being less worthy than their discovery. The result has been not so much an exaggeration of the importance of the laboratory, for its importance can hardly be exaggerated, but a relative minimizing of the value of study and investigation carried on outside of the laboratory. The time has now come, however, when we must devote greater study to this non-laboratory side. We must devote more time to investigating the patient. We must remember that he, too, is a laboratory in which actions are followed

by reactions. It is our duty to observe and investigate the patient with the same zeal and earnestness that our workers have been investigating his disease—its pathology, bacteriology and chemistry.

Then, too, this era through which we are now passing has been characterized by the development of mechanical methods of examination. The general tendency has been toward measuring things by the microscope, test-tube and mechanical devices, and away from study which depends upon man's power of observation. While these methods are extremely important and our modern scientific medicine has been established through them, yet there is something lacking which must be supplied if we will have medicine rounded out so as to meet the requirements of the patient. It seems to me that there are two outstanding needs in medicine today: (1) The correlation and unification of the recent scientific discoveries which have been made, and (2) more accurate clinical observation.

While all should know better, yet the opinion seems to be prevalent that laboratory and mechanical means of arriving at truth are accurate while clinical observation is inaccurate. To emphasize this opinion, laboratory and mechanical measures are termed methods of precision, intimating that clinical methods are naturally inaccurate. Nothing could be further from the truth. The laboratory and mechanical measures have back of them the errors incident to the reaction and the apparatus plus the errors of the observer; while clinical observation has the errors of the observer only. These I shall illustrate later in my discussion.

One cannot practise medicine alone by data obtained by the microscope, in the test-tube and through so-called apparatus of precision. The patient must be considered. There has been entirely too much of a tendency to reduce things to so-called normal standards. There can be no absolute normal as long as individuals differ as they do. Difference makes human beings interesting as individuals and makes their reactions differ in disease. He who tries to reduce all maximum daily temperatures to 98.6°; all pulses of men to 72 and of women to 80; blood-pressures during middle life to 130; and the time of the meal leaving the stomach to six hours is trying to practise medicine mechanically. He is omitting consideration for the most important element in disease, the patient who has it. This is the man who removes tonsils or sacrifices teeth if a patient has an ache, a temperature of 99° and a tired feeling without finding out the cause. He also condemns a nervous woman, with a blood-pressure of 180 to invalidism, simply on the blood-pressure reading alone.

It is now time to make advances. In order to do so we must evaluate these measures and learn what is error and wherein the error lies. One great error has been to think of tests apart from the patient tested; to think of each test as an entity when in reality it is

simply a procedure applied to some portion of the human body in order to determine certain of its characteristics.

Our rapid development has favored or made necessary specialization, and specialization in turn has hastened the discovery of scientific facts. Unfortunately it has also had a disintegrating influence upon medicine as a whole, for illogically it has divided the human body into parts and separated them from the whole.

One of the greatest criticisms that can be made of modern medicine is that all of this study along special lines, of individual diseases, individual organs and systems of the body and individual methods, has emphasized the part and minimized the whole. It has emphasized disease processes and methods of examination and minimized the patient. It is now time to realize the importance of the patient, to emphasize that the blood, urine and sputum examined in the laboratory, and the heart, lungs, eyes, throat and stomach which are now presided over by separate specialists all belong to a patient; and that the patient's organs and tissues are so linked together that every part is influenced by every other part and that every part influences the whole.

The necessity of correlation and unification then is self-evident. In order to do this we must know the patient and his reactions. The reaction of the normal individual belongs to the study of physiology, his reactions when ill, when a patient, belong to pathologic physiology. In the past it has been emphasized that the best clinician was the one who was well grounded in pathologic anatomy. This has probably been true, but I seriously doubt whether it will hold for the future. While diseases produce pathologic-anatomic changes in tissues, they also produce injuries to the organism which are recognized as symptoms. These symptoms are changes in function or pathologic physiology. Therefore the best clinician in the future will be the one who is not only grounded in pathologic anatomy but likewise in pathologic physiology; in other words, the physician who knows the disease and the disease process and at the same time understands the patient's normal and pathologic physiologic reactions.

It would be erroneous to say that clinical observation today is a lost art; it is the truth, however, that it has lagged behind other methods of investigation. It has not kept pace with laboratory investigation. Clinicians have been particularly remiss in not keeping themselves informed of discoveries in physiology. They have not learned to read the actions and reactions of patients in terms of physiology, which they must do if they would be good observers and accurate interpreters of their observations.

They must know and learn to recognize the differences in the patient's physiologic reactions in the presence of disease just as they have learned to know and recognize the pathologic changes as

revealed macroscopically or microscopically, or in the test-tube in the presence of disease. We would not hark back to the good old times in the pre-laboratory days when all there was in medicine was a doctor with common-sense and human feelings who knew only what he read in his patient; but we do look forward to the future when the practice of medicine will be based on an understanding which comes from a combination of facts derived from both laboratory investigation and accurate observation of the patient, interpreted by a mind which knows the patient no less than he knows the disease.

The principles herein discussed may be well illustrated in the development of our knowledge concerning tuberculosis. From the time of Hippocrates it has been the task of medical men to study tuberculosis. For centuries they groped in the dark, yet every now and then a new observation was made which materially increased the sum total of knowledge of the disease. At first knowledge depended almost wholly on observation of the patient, then later this observation was supported by crude pathologic observations; later by more accurate methods; but the greatest aid to progress during the last part of the eighteenth and the first part of the nineteenth centuries came when Auenbrugger, Skoda and Laennec made their contributions to the study of thoracic disease.

Louis in his preface to the second edition of *Researches on Phthisis* (1843) gives a splendid picture of the state of investigation at the time. He praised the researches of Bayle and Laennec as adding greatly to the knowledge of the subject but insisted that progress could be made only by recording and studying symptoms and then comparing them with the condition of the organs found after death, which is a correlation of the pathologic physiology with the pathologic anatomy. He recorded the number of times each symptom occurred in a group of patients and tried to analyze the patients in such a way as to explain why such and such a symptom was present in one patient and not in another.

He says: "I was led to the adoption of this method, designated as that of numerical analysis, not by choice, but naturally, involuntarily and necessarily, solely because I *seriously believed* what it has long been the fashion to repeat concerning medical science—namely, that it is a science of observation and observation purely." He then quoted Trousseau, who expressed his opinion of this method of medical study as follows: "I was one of the most violent and unjust detractors of this method; *I did not understand it.* Now that I have studied it I feel that it alone is capable of ensuring the solid advancement of our science, that it alone can enable the observers of one age to avail themselves to useful purpose of the labors of preceding ones, and slowly raise a structure which the reveries of a Galen or a Paracelsus must fail to overturn."

While these observers were rejoicing in the apparent security of methods based upon clinical observation and the study of the patient, developments were taking place which a little later were to withdraw attention from the patient and center it upon the pathology produced in the lung and the tubercle bacillus which caused the pathology. Then for a time clinical observation and study of the patient lagged and physicians became afraid to give an opinion on a case of suspected tuberculosis unless such an opinion was based on laboratory examination.

During the last few years an ever-increasing number of clinicians have been made to see the futility of depending on the laboratory for progress in the diagnosis of early tuberculosis. They are convinced that laboratory methods should be supplemented by more intense study of the patient; or what represents their opinion still better, they believe that intensive study of the patient should come first and that this should then be supplemented by laboratory study. The diagnosis should not depend on the laboratory findings, but the laboratory findings should be weighed along with those elicited by clinical methods and the diagnosis be based on the analysis and correlation of all data obtained. The diagnosis should be the result of a process of reasoning.

We shall now proceed to analyze the methods of diagnosis, particularly of early tuberculosis; for it is early tuberculosis that we must discover if we wish to make satisfactory progress in treatment.

The most useful and most commonly employed methods of examination for pulmonary tuberculosis are: (1) Clinical history; (2) physical examination; (3) examination of sputum; (4) roentgen rays; (5) tuberculin test; (6) complement fixation.

Of these, through clinical history and physical examination, the physician elicits data directly from the patient. The examination of sputum and complement fixation are wholly impersonal and the tuberculin test and roentgen rays are *quasi* personal. The roentgen rays might be classed as a laboratory method and the tuberculin test as a clinical method.

Sputum Examination. Of the purely laboratory methods we shall first discuss the examination of sputum: Sputum in suspected tuberculosis should be examined (1) for tubercle bacilli; (2) for the presence of albumin; (3) for lymphocytes. When tubercle bacilli are present in the sputum there is no question of the presence of pulmonary tuberculosis. This does not indicate, however, that the disease is active, for cases of old chronic quiescent tuberculosis will often show bacilli in the sputum, although no signs of clinical activity are present. In this they are tubercle bacillus carriers the same as certain patients are typhoid carriers. This is of interest mainly as a scientific fact and should not upset anyone's mind and make him worry, wondering if he has recommended patients for

care and treatment who did not need it. It is one of those facts in medicine which should be known but which will be employed infrequently.

The presence of tubercle bacilli in the sputum of the patients who present for chest examination, for all practical purposes, may be taken as meaning the presence of active pulmonary tuberculosis. Thus far this method of examination is of great value. On the other side, however, the absence of bacilli cannot be taken as meaning the absence of tuberculosis. Tuberculosis is often present, sometimes even in a widely scattered area, and at times may be causing marked clinical symptoms without the tubercles rupturing and bacilli appearing in the sputum. In fact, most patients show symptoms which to the alert diagnostician would warrant a diagnosis of active tuberculosis, before bacillus-bearing sputum appears. Secondly, the usual methods of diagnosis are subject to far greater error than is generally believed. I am surprised to find how generally the results are considered absolute for the specimen examined. Ordinary methods of treatment and staining sputum will detect bacilli if present in 2000 to a cubic millimeter. The most refined method with which I am conversant, that of homogenization, by treating the sputum with gasoline or xylol and shaking will enable one to find them if present in numbers of 200 to a cubic millimeter. Then, too, if a sample of sputum only is taken a great source of error creeps in, as patients with early tuberculosis may expectorate ten times a day, but expectorate bacilli only once; so, by a sample, the chances of failure would be nine out of ten.

For the examination of sputum in cases suspicious of early tuberculosis, it should be collected for twenty-four hours or for three days and homogenized before examination, otherwise the examination is unreliable. Even then the data are of no value in those cases in which tubercles have not yet broken down.

Sputum in cases suspected of early tuberculosis should also be examined for the presence of albumin. The presence of albumin, except in the smallest quantities, is suspicious of tuberculosis in patients who are not suffering from pulmonary abscess, bronchiectasis and the infected bronchi which are now so common since the influenza epidemic. When these are present they, too, produce the albumin reaction.

The presence of lymphocytes in the sputum beyond 30 per cent. is also suspicious of a tuberculous lesion.

The examination of the sputum is thus surrounded by more errors than are usually recognized.

Complement Fixation. Complement fixation is an immunity reaction but has many sources of error. It is theoretically positive in all cases of active tuberculosis. Practically, however, there are certain patients who have bacilli in the sputum who will not react,

and certain others who have slightly active foci without symptoms who will show a positive reaction. As an isolated test it would be unsafe to follow in diagnosis, but interpreted in conjunction with other data it is of value.

Roentgen Rays. The roentgen ray may be used to great advantage in the diagnosis of pulmonary tuberculosis. In order to be of value in the detection of early clinical tuberculosis, however, it should be operated and interpreted by those who are expert in its use; and, even in the hands of many of these the result is doubtful. I have my doubts whether it should ever, except in the hands of a real genius, be relied upon wholly for a diagnosis. In conjunction with other data it is very valuable. Aside from the purely scientific discussion of the question as to which method is the more reliable in the diagnosis of pulmonary tuberculosis, the roentgen ray or clinical examination, the roentgen ray has a great field of usefulness in the detection of comparatively early tuberculosis, and should be used generally and routinely in cases in which the clinician is in doubt. The diagnosis, however, should be made on data obtained by all methods of examination and not by the roentgen rays alone.

Tuberculin Tests. Personally I have had much more help from the various tuberculin tests than most of those who write on this subject indicate. Here, too, it is the interpretation after careful technic that counts. The tuberculin test like complement fixation is an immunity reaction. Immunity reactions are theoretically strongest when the body cells are busy combating antigen—that is, when the cells are fighting an active tuberculosis. Then they should produce more antibody, and this in turn, in coming in contact with the antigen artifically introduced, should produce a more marked reaction than when an active infection is not present. After comparing the tuberculin reactions in several hundreds of cases of suspected tuberculosis, with my opinion based on other methods, I find that a prompt marked reaction coincides closely with my opinion of clinical activity and a slight reaction or a delayed reaction coincides with my opinion of partial quiescence. I employ either the intradermal test, using $\frac{1}{10}$ to $\frac{2}{10}$ c.c. of a 1 to 5000 dilution of Koch's O. T. injected between the layers of the skin, or the cutaneous test using full strength of Koch's O. T. I prefer the intradermal.

This test must not be relied upon any more than the complement fixation and roentgen rays in making a diagnosis. It is only one source of obtaining information, but one that at times offers considerable aid. It should always be used in conjunction with the purely clinical methods.

It is evident from our discussion so far that these laboratory and *quasi* clinical methods have an important place in furnishing data to be used in the diagnosis of clinical tuberculosis. It is equally

evident that it would be unscientific and unwise to depend alone for diagnosis on any one of these methods. They should be interpreted only in conjunction with the data obtained by other and especially clinical methods. Unfortunately none of these methods gives an idea of the patient and the resistance which he is showing to the infection.

Clinical History. The clinical history elicits the various ways in which the normal physiologic processes of the body are disturbed. It is a physiologic inquiry. The facts are revealed either by the description of the patient—subjective symptoms—or by the perception of the observer—objective symptoms. No matter how revealed they express the manner in which the normal physiologic processes of the body have been disturbed.

This leads us to inquire how the physiologic processes of the body are controlled? So far as is known every act in the body is controlled either by the nerves or the endocrine glands; or by these conjointly; and these are subject to two classes of stimuli, physical and psychical.

Therefore in studying and interpreting symptoms it is necessary to know what there is in the disease, tuberculosis, which disturbs the nervous system and also what there is that disturbs the endocrine glands; and, further, in what way these stimuli act and what symptoms are produced by each. It can readily be seen that the symptoms of tuberculosis must vary according to the stability of the nervous and endocrine systems. This will make them differ in different individuals and in the same individual at different times. I recently observed a patient who developed an active clinical tuberculosis at the same time that she was developing a post-adolescent hypopituitarism. She gained some thirty pounds in spite of the early active tuberculosis.

In order to make our clinical observations of greatest value we must start with an adequate conception of the disease pulmonary tuberculosis and the manner in which it disturbs the normal physiologic action of organs. Starting with the conception that pulmonary tuberculosis is an infectious inflammation, chronic in nature, which (1) disturbs the nerve and endocrine balance of the patient and particularly produces sympathetic effects by toxins which are liberated from the disease areas, and in this manner produces general symptoms, and (2) irritates nerve-endings in the lung and in this manner produces reflex symptoms, we have a basis for explaining two groups of common symptoms found in this disease.

On this conception I have classified most of the symptoms of pulmonary tuberculosis into two groups, the toxic and the reflex. To these I have added one more in early tuberculosis, in which I place those symptoms which are incident to the disease itself; and still another in advanced tuberculosis in which are placed the symptoms and syndromes which result from the disease.

This classification is shown in the following groups:

SYMPTOMS OF TUBERCULOSIS IN GROUPS ACCORDING TO ETIOLOGY.

Group I. Symptoms due to toxemia.	Group II. Symptoms due to reflex cause.	Group III. Symptoms due to the tuberculous process per se.
Malaise	Hoarseness	Frequent and protracted colds.
Lack of endurance	Tickling in larynx	Spitting of blood.
Loss of strength	Cough	Pleurisy.
Nerve instability	Digestive disturbances (hypermotility and hypersecretion, which may result in loss of weight)	Sputum.
Digestive disturbances (hypomotility and hyposecretion)	Circulatory disturbances	
Metabolic disturbances, resulting in loss of weight	Chest and shoulder pains	
Increased pulse-rate	Flushing of face	
Night-sweats	Apparent anemia.	
Temperature		
Blood changes		

SYMPTOMS WHICH RESULT FROM PULMONARY TUBERCULOSIS.

Respiratory changes.
Dyspnea.
Circulatory changes.
Changes on part of nervous system.
Changes in blood.
General metabolic changes.
Degenerative changes.
Menstrual irregularities.
Other changes in internal secretions.

When the symptoms are analyzed and grouped in this manner they have a very different meaning from that which is attached to them when treated individually. The presence or absence of certain symptoms and the presence of certain ones in combination give a basis for not only suspecting a tuberculous process but for judging whether or not it is active.

If we discuss the meaning of these groups we see that Group I is made up of some of the very common symptoms of active tuberculosis; but it is necessary to emphasize the fact that these symptoms varying in their combination and in the degree of their severity are not pathognomonic of the toxemia of tuberculosis, but are the same though differing in severity, in all toxemias. Many of this same group may be present in cases of nerve or endocrine unbalance and many of them are due to overwork. So there is nothing in this group when taken alone upon which we may base a diagnosis of active tuberculosis. It is a group due to general nerve and endocrine disturbances and when due to active tuberculosis is indicative of toxemia.

Those symptoms found in Group II are due to reflex action. They are caused by the inflammatory process in the lung acting upon the sensory fibers of the vagus and sympathetics and sending impulses centralward to the medulla and cord and there transferring

them to the nerves which go to other structures to produce action. This group contains those symptoms which are usually designated as "functional." It is characteristic of them that the impulse arises in one structure and the disturbed function occurs in another. It will be noticed that all of these symptoms point away from the lung; the first three point to the larynx, the fourth to the gastro-intestinal canal, the fifth and seventh to circulatory disturbances and the sixth to skeletal structures.

There is nothing in this group which, when taken alone, would warrant a diagnosis of active pulmonary tuberculosis; but when those symptoms on the part of the larynx are combined with symptoms of Group I lasting more than a few days or lasting a few days and recurring, then we feel quite sure that the cause is not in the larynx but in the lung. Digestive disturbances associated with symptoms of the toxic group are very suggestive, and especially if laryngeal irritation is present. Flushing of the face with cough is especially suggestive and will nearly always be accompanied by toxic symptoms. Chest and shoulder pains, particularly the dull aches, are suggestive but need other symptoms to point to activity.

The symptoms in the last group (Group III) are due to the tuberculous process *per se*. This may not be a happy designation for this group, but it has the recommendation of being suggestive.

Frequent and protracted colds of tuberculous origin are accompanied by other symptoms of Groups I and II, and from their frequency or the fact of their repetition may be considered as being due to a chronic process, the most common of which is tuberculosis.

Spitting of blood should always be considered as being due to tuberculosis unless another cause is obvious. In this I do not mean a streak or a speck of blood, but free, bright blood. This symptom may appear unaccompanied by others; but, as a rule, if of tuberculous nature, will have some symptoms of Group I and II or others of Group III, precede, accompany or follow.

Pleurisy either dry or accompanied by effusion is usually of a tuberculous nature. It is nearly always accompanied by laryngeal irritation, often by flushed face, and usually by some of the symptoms of Group I. It always means active tuberculosis and should be heeded as a sign of such.

Sputum may be a result of the stimulation of the mucous glands of the bronchi by the tuberculous process or consist of the secretions from ruptured tubercles. If due to tuberculosis it is usually accompanied at least at times by laryngeal irritation and other reflex symptoms and some of those belonging to Group I.

It can readily be seen that the most important group of symptoms from the diagnostic point of view is Group III. It is further evident that few of these symptoms occur alone. They are usually so combined as to make the meaning quite plain if carefully analyzed. By eliciting a careful history, and following this group of symptoms

little doubt should remain in the examiner's mind as to the presence or absence of active tuberculosis; and the valuable part is that the diagnosis can usually be made before bacilli appear in the sputum.

Physical Examination. The data obtained on physical examination above all other methods is based upon the observation and skill of the examiner. In it he aims to determine what pathologic processes are present by methods which reveal disturbances in the normal anatomic and physiologic condition.

The changes which are found on physical examination are usually discussed as though they were anatomic disturbances; but such is not the case. They are partly anatomic and partly physiologic, and the physiologic changes, if one understands that part of visceral neurology which pertains to the lung and pleura, are just as definite as the anatomic changes.

Auscultation and percussion have long been depended upon as affording the best diagnostic data in pulmonary tuberculosis. This is partly due to the fact that it is generally believed that the examiner is examining the lung tissue more directly than in any other manner. When one considers all the difficulties and errors which are incident to these methods in early cases of tuberculosis, he is forced to the conclusion that the data obtained through them would be much easier of interpretation if substantiated by data from other methods. This is why other methods have been searched for so diligently.

I desire in the remaining portion of this paper to discuss certain physiologic changes which result from the infection in the lung which furnish this corroborative evidence, or which may be taken as giving primary evidence to be corroborated by the findings on auscultation and percussion.

There has been a tendency in examining chests to direct the attention too much to the changes in the lung. While these are what we wish to determine, yet we must not consider that we can auscultate and percuss the lung alone. The percussion note is made up of vibrations set up in all of the tissue which come in the path of the percussion impulse and is modified by all adjacent structures, even the surroundings of the patient. Therefore percussion examines the skin, subcutaneous tissues, muscles, bony thorax, lung and all adjacent structures which modify the impulse. The tension of the soft tissues as revealed, especially in the degeneration of the subcutaneous tissue and muscles and the increased muscle tone, often make up most of the departure from normal in the percussion note. This is particularly true in percussion over the apices from the second rib upward in early tuberculosis. When active pulmonary tuberculosis is present the scaleni, which are inserted in the first and second ribs, the sternocleidomastoideus, which is inserted in the sternum and clavicle and the pectoralis which is spread out over the surface of the ribs, all show increased tension; and so produce a fixing of the upper portion of the chest

wall. Percussion through this fixed area and through the tense muscles must of necessity produce greater changes in the percussion note and percussion resistance than can possibly be produced by the few tubercles in the lung. Personally I believe this causes the major portion of the percussion changes that we have been ascribing to the infiltration in the lung in early tuberculosis.

This same is true of auscultation though to a lesser degree. The changes on auscultation are not all due to the modifying of the sounds in the lung. The muscles, subcutaneous tissue, ribs and other structures change and modify them, too. One hears a murmur not wholly unlike that due to respiration over contracting muscles. In complete pneumothorax and empyema the chest wall with its coverings gives fair imitation of the respiratory murmurs, although there is no pulmonary tissue underlying. Examiners must not concentrate too much on the lung but must consider all adjoining and modifying structures.

In passing I should like to call attention to an almost wholly unknown and neglected method of diagnosis which depends upon anatomic change for its value and which in my hands has proved of great value. I refer to palpating or feeling the anatomic changes in the lung. Palpation is as accurate as percussion at its best without being subject to so many errors. Different density in the lungs, mediastinum and pleura may be felt by a light palpation—light touch palpation. Infiltration, empyema, cavity, pleural exudate, thickened pleura, the borders of the lungs, the heart and the liver may all be detected by palpation; in fact, everything that can be detected by percussion, and some of it without the error that is incident to the percussion stroke which sets up vibrations extending to adjacent structures. One palpates or feels more directly than he percusses. Aside from this method being of great value in diagnosis, it offers proof of the superiority of light over heavy percussion.

There are certain disturbances in physiologic action in pulmonary tuberculosis which are visible to the eye and recognizable on palpation. I refer to the motor and trophic changes in the muscles, skin and subcutaneous tissue, which are reflexly produced by the inflammation in the lung. These reflexes are of especially great diagnostic import because they affect skin and subcutaneous areas and groups of muscles which are distinctive. Barring the diaphragm there is no other organ, except the heart on rare occasions, which produces reflexes in these structures.

The structures which show the pulmonary motor and pulmonary trophic reflexes are as follows:

1. The pulmonary motor reflex expresses itself in those muscles which receive their innervation from the cervical segments of the cord, particularly the sternocleidomastoideus, scaleni, pectoralis, trapezius, levator anguli scapulæ, rhomboidei and diaphragm.

2. The pulmonary trophic reflex is shown in the skin, subcutaneous tissue and muscles supplied by the cervical segments of the cord, particularly the III, IV and V segments. This means the skin and subcutaneous tissue from the chin to the second rib anteriorly and from the base of the skull to the spine of the scapula posteriorly; and the muscles belonging to the shoulder girdle, and the diaphragm, as mentioned above.

This pulmonary reflex is produced by impulses arising in the inflamed lung. They are carried to the cord by the sensory sympathetic neurons and there transferred to ascending neurons which carry them up into the cervical part of the cord and these again transfer them to motor and sensory spinal nerves which supply the tissues above mentioned as the seat of the reflexes. The cause of these reflexes is identical with those which are so well known in connection with the appendix, gall-bladder and stomach, except that instead of the afferent impulse which is carried to the cord finding efferent motor and sensory nerves in the same segment with which to complete the reflex, in case of the lung, it must be transferred upward in the cord to the cervical segments. This variation is based on embryologic differences.

The motor reflex which shows an increased tonus (spasm) of the muscles may be seen on inspection or detected by palpation. It may also be detected by the effect which it produces in limiting the respiratory movement. On inspection of the muscles themselves, particularly the sternocleidomastoideus, trapezius, levator scapulæ and rhomboidei they may be seen to stand out more prominently than normal and on palpation they reveal an increased tonus or spasm. This increased tonus is also detected in the scaleni. The effect of the reflexes is to shorten the muscles, and this shows in a limitation of movement. This is particularly produced by the scaleni above and the diaphragm below. That the infiltration itself in reducing the elasticity of the tissue of the lung particularly in advanced cases, is also a factor in lessened motion is quite probable; so are pleural adhesions either at the base or elsewhere; but this lessened motion often appears early in the disease when the amount of tissue involved is scarcely sufficient to be considered, and when pleural adhesions do not seem to be present; at a time when the only factor which seems capable of producing it is the reflex muscle tension.

These two symptoms then, the increased muscle tonus, particularly as detected on palpation, and the lessened respiratory movement, are just as much symptoms of physiologic disturbance as are the symptoms detailed above under the discussion of clinical history. As such they are among the most evident, therefore most dependable, symptoms indicative of active inflammation in the lung; and because of their localization in definite groups of muscles their presence suggests pulmonary disease.

The pulmonary trophic reflex shows as degeneration of these same muscles and of the skin and subcutaneous tissue above the second rib anteriorly and the spine of the scapula posteriorly. This is indicative of chronic inflammation and would be of no value in the diagnosis of early tuberculosis were it not for the fact that clinical tuberculosis usually manifests itself long after the lung tissue has been invaded. Chronic inflammation means chronic stimulation, and this results in injury to the neurons in reflex relationship to the parts inflamed. This results in trophic change, lack of nutrition and degeneration. These degenerations, then, which are evident at a glance and more so on palpation, tell at once that the patient under observation has probably had a chronic inflammation in the lung. Tuberculosis is the one chronic inflammation which produces the greatest amount of reflex degenerative change, although chronic infected bronchi, unresolved pneumonia, pulmonary abscess and other chronic infections produce some. If the history gives no evidence of other conditions, or if the degeneration is marked, the evidence is strong of tuberculous infection being in the underlying lung. Degeneration in these tissues when symptoms suspicious of active tuberculosis are noted, now that we know the tendency for old infections to become reactivated and furnish foci from which the disease may spread, offers valuable diagnostic suggestions; and if accompanied by spasm in the muscles of the shoulder girdle practically makes a diagnosis of a reactivated tuberculosis.

Diagnosis is a process of reasoning. It is not made on one thing alone. Relationships between cause and effect must be seen and appreciated. Data must be carefully considered and correlated.

From our discussion we can see how advantageous it would have been had clinical observation kept pace with laboratory research during the period of development of our knowledge of tuberculosis; and with our knowledge brought to its present state, the one outstanding cry is for more thorough clinical study. It now offers the greater and apparently the more fruitful field. The patient should be studied more intently and his body reactions should be recognized and interpreted with greater accuracy. Without belittling in the least the magnificent work produced by the laboratory I wish to assert with emphasis that no laboratory method alone or no combination of laboratory methods will ever give the clinician a knowledge equal to that which comes from observing and analyzing the patient. Looking into the future we have an increasing confidence that clinical observation and research will be prosecuted with greater zeal and that it will produce a better balanced science of medicine and one which will be better able to satisfy the requirements of the patient.

PSEUDO-RUBELLA.[1]

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During the last ten years of practice among infants and young children it has been the fortune of the writer to encounter, at more or less considerable intervals of time, isolated cases of a febrile eruptive malady of infancy which have so closely resembled each other in general characteristics as to suggest the definite symptom-complex of a mild infection resembling, but apparently differing from, rubella in several important features.

This pseudo-rubella, as it may be called for the present, seems to be confined to infants between the age of eight or ten months and twenty months to two years, and in every instance observed has occurred in private practice in children who have in the majority of the cases had older brothers and sisters to whom a disease of the contagious character of rubella could easily have been communicated. In not one of the 10 cases observed has the attack been preceded by a similar affection or by rubella in the other children of the family, nor has any instance of communication of the disease or of rubella to other children been observed. The resemblance to a mild rubella has been so striking that this diagnosis always has been most carefully considered, and in each case efforts were made to trace possible exposures to this contagion but without success. While this failure is not remarkable, the absence of communication of a similar disease or of rubella is certainly noteworthy.

These cases have always been observed singly and unexpectedly, never during the prevalence of an epidemic of rubella, and have recovered so promptly that little opportunity has been offered for exhaustive study other than careful noting of the clinical features; and it is therefore with the hope that others may have wider opportunity of observation that the writer ventures to present this purely clinical paper.

The characteristics of rubella are well known. Most writers speak positively of the absence or short duration of prodromal symptoms; of the usually slight degree of fever, which may range, however, from normal to 103° or 104° F. and of the prompt appearance of the rash, frequently the first distinct evidence of the disease. D. J. M. Miller[2] has called attention to the fact that a febrile pre-eruptive stage lasting three or four days or even up to six or seven days might occur, with prompt fall of temperature after the eruption appeared, and this has been confirmed by others, including

[1] Read before the American Pediatric Society, Washington, May 10, 1916, and not previously published.

[2] Archives of Pediatrics, January, 1905.

the writer; but, as these cases certainly are exceptional, it would seem more reasonable to attribute them to a delayed appearance of the rash, rather than to a prolonged prodromal stage.

The eruption of rubella appears as small, round, rosy-red macules or maculopapules, first behind the ears, on the scalp and face, and thence spreads rapidly downward over the body; the spots become larger and in some areas coalesce to form patches of the so-called "bat-wing" pattern. The enlargement of the post-auricular and postcervical lymph glands, and frequently of the axillary and inguinal groups, and occasionally of isolated glands over the abdomen and chest, is one of the most distinctive features of rubella. Desquamation is very variable, sometimes is entirely wanting; but usually can be detected by close observation in the form of fine powdery scales.

The onset of pseudo-rubella is abrupt. The infant, previously in perfect health, is found usually toward evening to be feverish, fretful, may refuse his bottle, or may even vomit once or twice. The temperature is elevated, 102° or 103°. If seen at this time, examination shows normal fauces, a clean or only slightly frosted tongue, with a normal or only slightly feverish odor to the breath. The pulse is somewhat accelerated, in keeping with the rise of temperature, but of good quality and not suggestive, while the heart sounds are clear. The lungs are negative; there is no cough nor coryza, no lacrymation nor conjunctival irritation, no abdominal symptoms; the last stool of perfectly normal color and consistency. The spleen and the liver are not enlarged. The external ears and surrounding tissues are not tender to touch, and the speculum shows perfectly normal drumheads. Under these conditions a positive diagnosis is impossible. The possibility of a latent intestinal disturbance, however, will prompt the administration of a laxative like castor oil, with the result on the following day of a good clearing out of the bowel showing normal intestinal contents modified only by the changes resulting from the hasty clearing out of milk feces that have not had time for complete digestion—a normal castor oil stool. On the second day the febrile elevation continues, 101° to 102° in the morning. Physical examination yields nothing new except the observation that the postcervical chains of lymph nodes are palpable and seem to be slightly tender. The post-auricular glands are not affected, but in some of the cases the inguinal nodes have been found slightly enlarged. The axillary glands have not been involved.

The evening temperature is fairly high—103° to 104°, but the baby usually takes food better and is grateful for water. The diagnosis, except for a possible mild rubella, seems no clearer than at first. The third day is very much a repetition of the second, the morning temperature usually somewhat lower, averaging about

101°, while the evening temperature may reach 104° and over, but no more conclusive symptoms have made their appearance, except for the possibly greater prominence of the lymph nodes.

The urinary examination shows no abnormality. The pulse is still elevated, but the baby seems brighter despite his fever, and shows no signs of toxicity. There have been no changes in the mouth or fauces, no enanthem, and no abnormal physical signs in the rest of the body.

The diagnosis is therefore still in doubt; and prompted by the enlarged postcervical glands, one is tempted to speak of rubella and to look for a rash without success. The fourth day still shows fever about 102° in the morning, with no new symptoms; but toward evening, with the temperature usually not so high as on the preceding evening, a few discrete pale reddish macules, about the size of the head of a pin, may be observed variously about the neck, on the face, under the ears or above the clavicles.

On the fifth day the temperature is about 101°, the rash has come out rapidly since the evening before and covers more or less thickly the face, neck, chest and shoulders, and is spreading downward. It is more discrete than a typical rubella rash, not raised above the surface but in some areas on the face has grouped or coalesced into roundish patches of the size of a very small coin. This tendency to coalescence is also noticed about the loins and in some cases about the thighs. The arms and legs are but sparsely invaded, and the palms and soles are usually spared. The color is pale pinkish, even slightly violaceous. The temperature keeps falling, often to below 100° by evening, and the pulse comes down. The baby is brighter, takes his bottle better and passes a good night.

The following day the temperature and pulse are practically normal. The rash is still present, but looks less intense. The enlarged glands are noticeably smaller and less sensitive. There have been no catarrhal symptoms, no changes in the stools. Except for the rapidly fading rash and still enlarged glands, the baby is well. An occasional transient concentration of the urine, and exceptionally a passing trace of albumin without casts have been noted, but the urine has always cleared up rapidly.

In a day or two the rash has disappeared, leaving phantom traces of discoloration for a few days. The glands have been reduced to almost impalpable size and soon cease to be noticeable. No desquamation has been observed in any case.

The resemblance to rubella is therefore quite striking, especially in the characteristic appearance of the rash, the enlargement of the postcervical glands and the febrile course; but there are a number of points of difference which must be carefully weighed.

Contagion.—Rubella is decidedly contagious, prevailing in epidemics and rarely seen sporadically. It is also generally accepted that second attacks are exceedingly rare. None of the infants of

the series here reported, all of whom were of well-to-do families, had been known to have been exposed to rubella, nor did any of the cases occur during or shortly before or after an epidemic prevalence of this disease. While susceptible children in the same household have in a majority of the cases been in contact with the patient before the appearance of the rash, and even during the whole course of the illness, no instance of a secondary case has occurred either in the same family or among other possible contacts. The cases have occurred sporadically, usually widely separated in time, most of them in Philadelphia, two of them at an interval of a month during the same summer at Cape May, N. J., these latter, however, in two families unacquainted and not living near each other.

Only one of the infants of this series, who had had "pseudo-rubella" at the age of two years, is known to have had an attack of rubella subsequently, at the age of nine years; but, for the other cases, it may be pointed out, the more rigid rules of the Board of Health of Philadelphia, which now quarantines rubella equally with true measles, may well account for an escape from rubellous infection up to the present time.

Age.—The general consensus of opinion, gleaned from an exhaustive study by Griffith[3] in 1887, seems to be that rubella occurs especially between the ages of five and fifteen years, though it has been seen in children under two years (Griffith), and Scholl[4] reported a case in an infant a few days after birth, the mother having had the disease two months before her confinement. All the children in the series here reported were under two years of age.

Invasion.—Many of the cases of rubella collected by Griffith in the monograph already quoted showed no prodromes at all. In a large number, however, slight symptoms were observable for not more than twelve hours before the rash made its appearance. His conclusions, from a comparison of numerous published reports, are that the symptoms in a normal case are malaise, often slight cough, suffusion of the eyes with some lacrymation, probably some coryza, sometimes pain in the limbs, drowsiness, at times hoarseness, sore throat often, enlargement of the glands at the back of the neck and behind the ears, possibly an elevation of temperature of 1° or 2°, occasionally nausea, and some edema of the face.

In the series forming the basis of this study the invasion has lasted invariably three full days or somewhat longer from the onset of fever to the first appearance of the rash and the rapid decline of temperature. There has been no cough, no suffusion or congestion of the conjunctivæ, no coryza or other catarrhal symptoms, no angina, no enanthem.

Eruption.—While the rash of rubella is rose-tinted in color, of a distinctly brighter hue than the darker red of true measles, the

[3] Medical Record, July 2 and 9, 1887.
[4] Trans. Med. Assoc., Alabama, 1881, p. 528.

enanthem in the cases of this series was paler, less rosy and even in several instances with a slightly violaceous tint. It was less liable to coalesce into larger areas especially where folds of the cutaneous surfaces occur, and was therefore more discrete, and spread more slowly to lower parts of the body. It had little or no elevation above the surface, and in no case presented an appearance simulating that of the scarlatiniform type of rubella.

Allowing for the long intervals of time between the individual cases observed, it has seemed that the rash has faded more rapidly and has left less pigmentation than does rubella. Desquamation has been observed in none of the cases.

Symptoms of the Eruptive Stage.—The absence of angina and enanthem and of the catarrhal symptoms so frequently found in rubella leaves the eruption and the adenitis as the only features of the eruptive stage, since the fall of temperature is very prompt as soon as the rash appears; while in rubella fever is usually an important symptom of the eruptive stage and in a considerable number of cases an elevation of from 99.5° to 100° has continued for a week after the rash has entirely vanished.

Tenderness and enlargement of the lymph nodes, while invariably found in all the cases of this series, was never so widespread or so marked as in rubella or in "the fourth disease," as described by Dukes, who states that the enlargement is universal in both diseases. In the pseudo-rubella cases enlargement was chiefly confined to the postcervical chains; but it is important to emphasize that enlargement and tenderness were present very early in the prodromal stage and rapidly subsided as soon as the eruption appeared.

The Fourth Disease.—From the "fourth disease" of Dukes pseudo-rubella is distinguished by its long prodromal period as compared with that of a few hours (Dukes), by the slower progress of the eruption, by the characteristics of the rash, the absence of throat symptoms and its marked difference in general appearance from scarlet fever, which the "fourth disease" is considered to resemble so closely as to cause frequent confusion of diagnosis; and, finally, by its apparent lack of contagiousness and the absence of desquamation, both of which features are marked in the "fourth disease."

It is therefore evident that enlargement of postcervical lymph glands, fever, and a rash are the only symptoms common to true rubella, pseudo-rubella and the "fourth disease," and that while a diagnosis of rubella would have been the most natural one to make in the cases here reported, sufficiently sharp distinctions have been noted in the clinical picture to warrant the suggestion that they were not rubella, and certainly not the so-called "fourth disease."

The conclusion therefore seems reasonable that this symptom-complex constitutes a hitherto undescribed mild infection, non-contagious, or only feebly contagious, to which young infants are

peculiarly susceptible and older children not at all or only rarely liable.

If, as the writer believes, these cases are not true or modified rubella, it is important that the existence of a pseudo-rubellous affection of young infants should be recognized, and by reason of its non-contagiousness should not be subjected to the quarantine that properly is enforced by health authorities against true rubella.

CLASSIFICATION OF RALES: A PLEA FOR SIMPLIFICATION.

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The writer has taught physical diagnosis for many years. He is impressed with the difficulties encountered in teaching students to identify the adventitious sounds heard in auscultation, commonly called *rales*. He has examined most of the text-books in use in the leading American universities and finds an astounding divergence in the matter of nomenclature. The variation, so far as the student is concerned, depends to a very great extent on the early educational environment of his teachers or of those who have written the text-books that are put into his hands for study.

It is quite desirable that the student come into contact with men who have themselves been taught in different schools. This gives the student a little broader grasp of his subject than he would get otherwise. However in respect to this part of the nomenclature of physical diagnosis the difference in teachers may bring confusion to the student.

Seldom do we find two authors whose classification is the same. Every writer has apparently been conscious of the difficulty and has tried to make a classification which will clarify the situation. They have all failed to do this. My own effort may meet with the same failure, but if calling attention to the difficulty may result in some sort of coördinated effort to remove obstacles for the medical student I shall be content.

He may be spared the supreme memory effort of mastering such a list as the following, taken from the authors I have had at hand: Dry, moist, sonorous, sibilant, mucous, submucous, crepitant, subcrepitant, wheezing, whooping, mucous click, crowing, whistling, piping, squeaking, hissing, humming, high-pitched crackling, bubbling, small bubbling, gurgling, snapping, musical, coarse, fine, resonant, non-resonant, consonating, non-consonating, flapping, cardiopneumatic, laryngeal, tracheal, cavernous, euphonic, pleural, vesicular, latent, crumpling, crackling, metallic groaning, hollow,

metallic tinkling (*Gutta cadens*), bronchopulmonary, fistula rale, crepitous, indeterminate, frémissement cataire, Hippocratic succussion.

Our first classification came from Laennec, as we all are aware, and it is today superior to the classifications found in most of the text-books. He did not use the word *rale* but the French word *rhonchus*. I quote from the translation by Forbes[1]—Rhonchi (rales).

1. Moist crepitus rhonchus or crepitation (very large).
2. Mucous rhonchus or *gurgling* (large, middling, small).
3. Dry, sonorous rhonchus or snoring.
4. Dry, sibilous rhonchus or whistling.
5. Dry, crepitous rhonchus, with large bubbles or crackling.

Those who came after Laennec in their effort to supplement and clarify the work of the master have gone further and produced the almost Rabalaisian collection I have mentioned above.

Professor G. Andral in his notes on the fourth and latest French edition of Laennec has the following to say regarding rhonchi (rales): "Since Laennec hardly anything has been added to the excellent description given by him of the different rhonchi." Surely it is commendable that study of such an important contribution should go on, that a form should be determined and some sort of agreement reached as to terminology to which we shall all agree. It is within the province of constituted medical associations to aid in clarifying matters of this kind.

It would seem important that medical men who speak the English tongue adopt a standard terminology.

The diagnostic value of the signs and the importance of their differentiation are not to be gainsaid. Who will deny that the determination of a different type of rale speaks for a difference in pathology? Yet how frequent is it that we read in medical papers, "Rales were found at the base?" The authors who write thus evidently are choosing words which all understand and prefer not to enter a discussion as to classification. Perhaps they are wise.

In a survey of the literature we find two tendencies. One school, among which that of Austin Flint[2] stands out conspicuously, has attempted to establish a nomenclature based on anatomical considerations. Austin Flint's classification is as follows: Laryngeal and tracheal rales; bronchial rales; vesicular rales; cavernous rales; pleural rales; indeterminate rales.

Flint uses the term "so-called" as applied to the *subcrepitant* rale in the chapter on classification of rales and attributes great diagnostic importance to this rale. One gets the impression that he accepts the term against his will. Indeed, his idea in departing

[1] A Treatise on the Diseases of the Chest and on Mediate Auscultation, by R. T. H. Laennec, M.D., 3d French edition. Trans. by John Forbes. Samuel S. and Wm. Wood, 1838.

[2] Auscultation and Percussion, 6th edition. Lea & Febiger, 1912.

from Laennec's original classification is set forth on page 140, "The term *subcrepitant* gives rise to confusion and there is no advantage in retaining it as the name of a distinct sign. Very fine bubbling expresses more correctly the characters of the sign. The moist rales are often called *mucous rales*. The name is obviously inappropriate, since not only are the sounds produced by other liquids than mucus, but other liquids are best suited for their production, especially in the large and medium sized tubes."

One of the difficulties in classification comes from the limitation of the words "mucous rales." If we take it in the narrow sense of a rale produced by a mucous liquid, all that Flint says is true. However if we consider the word as applying to a rale produced in a tube lined with mucous membrane we are justified, perhaps, in preserving it. Flint's subclasses describe vividly the acoustic qualities used by Laennec's *sonorous* and *sibilant*. Yet he avoids the words.

Da Costa the elder[3] uses a strictly anatomical classification: Bronchial; vesicular; cavity.

His subclasses are made by acoustic qualities and are of the simplest. All of the types of Laennec's main headings are here preserved, namely, *sonorous, sibilant, mucous, crepitant.*

The younger Da Costa[4] puts forth a classification based partly on anatomical and partly on auditory qualities. This is fatal to understanding and to good pedagogics. Here, in the writer's opinion, is the source of most of the confusion which exists.

We have another classification which is partly based upon the physical properties of the apparatus producing the sound and partly on the auditory perception of the sound itself.

In explanation of dry rales Sahli[5] says they may have their origin in *viscid fluid*. This shows how artificial is the term and impossible from the standpoint of clearness. In justification of the term "bubbling," Sahli says: "The term 'bubbling' was employed because it was formerly supposed that moist rales arose from the bursting of air-bubbles in fluid secretion. Of course, we know now that the contents of the bronchi are not sufficiently fluid for such an explanation, and so we suppose that the rales arise from *membranes* of *secretion* being formed in the bronchial lumen and then torn apart again, partly by movement of the air and partly by movement of the lungs." If the term *moist* does not mean moisture or fluidity of tube content, if a dry rale may have its origin in *viscid fluid* are we justified in further burdening medical literature with either of these terms?

Norris and Landis[6] say in explanation of a classification purely

[3] Medical Diagnosis, 1898. J. B. Lippincott & Co.

[4] Principles and Practice of Physical Diagnosis, 4th edition. W. B. Saunders Company, Philadelphia, 1919.

[5] Treatise on Diagnostic Methods, Trans., 4th German ed. Kinnicutt & Potter, 1905. W. B. Saunders Company.

[6] Diseases of the Chest and the Principles of Physical Diagnosis. W. B. Saunders Company.

auditory in character: (Sonorous; sibilant; crepitant; subcrepitant; bubbling.) "Genetically all rales are moist but sometimes they are classified as 'moist' and 'dry.' These are undesirable terms, however, and should not be used. Further, the term 'dry' as applied to rales seems paradoxical, for it is impossible to conceive of a 'rale' that does not, to some extent at least, depend on moisture or increased turgescence for its causation."

I heartily agree with this conclusion.

Upon the classification moist or dry, Latham[7] makes this illuminating statement: "Call it *rale* or *rattle* or *crepitation* or what you will, but pray do not add 'mucous' to it by way of specific difference, for this term must always imply that the sound is produced by air passing through mucus whereas it is produced equally by air passing through mucus, blood or any fluid whatever. Besides, it is beyond the truth to say that the quality of the fluid through which the air passes can be distinguished by the quality of the sound that results. The sound will indicate the situation and quantity of the fluid and no more."

We are indeed fortunate for this, for most of us believe that the situation and quantity of the fluid may be estimated by the extent and quality of the rales heard after our ears are trained to recognize them. In listening and learning we must teach our students to see the structure of the region examined and to picture the mechanism of the production of the rale heard rather than to identify a certain auditory quality for which he must endeavor to find a name. If we insist on an anatomical classification this power will come to the student.

Richard Cabot[8] has departed furthest from the classic nomenclature of Laennec. He has done this without utilizing the anatomical classification of Flint. All of the classical terminology has been abandoned with the exception of *crepitant*. Nowhere do we see mention of *mucous*, *subcrepitant*, *sonorous* or *sibilant*—terms certainly as worthy as *bubbling*, *crackling* and *musical*. Cabot even mentions "complicated chords from rales which vary in pitch." One reads and fears that tomorrow may bring forth the necessity of adding harmonics to an already full junior year.

Of all the authors cited, Sam J. Gee[9] has, perhaps, adhered more closely to the original of Laennec in the matter of classification. In his foreword he says: "The sense of words has not been perverted nor have new words been introduced to denote signs already well denominated. Much of the difficulty of teaching auscultation and percussion to students is due to neglect of these plain rules." Gee utilizes but four categories: Crepitant; mucous; sonorous and sibilant; doubtful.

[7] Lectures on Subjects Connected with Clinical Medicine. Philadelphia, Borrington, 1847.

[8] Physical Diagnosis, 6th edition. Wm. Wood & Co., 1915.

[9] Auscultation and Percussion, 6th ed., London.

In starting out to write this paper I was thoroughly convinced that any departure from the classical terminology was to be deplored. Since examining and tabulating the classifications from various sources I am convinced that there is no need to sacrifice the advantages of an anatomical classification to this end. If we take three simple heads: (1) Crepitant or vesicular; (2) mucous or tube; and (3) cavernous we shall be able to place every rale we hear excepting pleuritic friction sounds, which are perhaps best excluded from this category.

It may be that I may be charged with perverting the meaning of the word "mucous." It is surely within a tube lined with mucous membrane that these rales have their origin. Whether fluid or tenacious, the basis of the mechanism which produces them is mucous; whether they are due to turgescence of the lining of the tube, or to muscular contraction in the wall, our term applies. We can utilize the classical *subcrepitant* and the onomatopoetic pair *sonorous* and *sibilant* as subdivisions of the *mucous*. Nearly all of the half a hundred of varieties described by the authors named and others would be subvarieties of the mucous rale.

Of the other two, one (*crepitant*) stands alone and needs no comment or word of explanation. The other (*cavernous*) I should perhaps include within the category of mucous rale also. This would be a further and a desirable simplification. We should then have but two categories: (1) Vesicular or crepitant rales; (2) tube or mucous rales. This shortening involves no departure from Laennec's form other than placing *sonorous* and *sibilant* as subheads of mucous and the addition of the corresponding anatomical words.

I feel sure that teachers and students would rejoice if but two great classes of rales were to be remembered.

THE DIAGNOSIS OF PRIMARY LUNG TUMORS.[1]

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Until comparatively recently the lungs have been an unexplored surgical domain. Improvement in method of anesthesia and in the technic of thoracic surgery have enabled the surgeon to invade the lungs with rapidly increasing success. The time is not far off when thoracic surgery will be just as common and the thorax invaded by the surgeon with the same ease as the abdomen is today. The development of this hitherto untrodden surgical field imposes upon the internist the duty of recognizing intrathoracic lesions that

[1] Read at a meeting of the Yorkville Medical Society, February 20, 1920.

may be amenable to surgical treatment much earlier than was previously necessary or customary.

We shall confine our remarks in this paper to the medical diseases of the lungs which are amenable to surgical treatment. Essentially such lesions consist almost entirely of lung tumors.

Tumors of the lungs may be either secondary or primary. We shall discuss the secondary tumors first as they are much more common and comparatively easy to recognize, but hopeless from the therapeutic standpoint. However, they are apropos in this discussion because their clinical features throw a good deal of light upon the primary lesions of the lungs. The diagnosis of these secondary metastases of the lungs does not present many problems. Nevertheless it is surprising how often the condition is overlooked. The most important diagnostic feature of the secondary metastatic lung tumors is, of course, the etiological factor. This is the history of a previous removal of a primary lesion, in the breast, in the stomach, in the eye or other organ; or, as is not infrequently the case, the actual but unrecognized presence of the primary lesion at the time the patients present themselves for examination.

Besides the history of this etiological factor the patient complains of progressive cough and expectoration, which may or may not be blood tinged, of dyspnea, cyanosis, pain in the chest and loss of weight. At the same time there may be symptoms of other metastases such as pains along the arm and forearm from axillary nodes or pain in the back and along the extremities as evidence of spinal metastases.

The examination of the chest may reveal areas of localized crepitant and subcrepitant rales or signs of fluid in one or both chests. The character of the fluid on aspiration is of extreme importance. A bloody fluid in the chest is very suggestive of metastasis in the lung, but the fluid does not become bloody unless the metastases are very extensive, and consequently the presence of a serous fluid in the chest does not exclude malignancy. The roentgenographic examination may show scattered shadows in one or both lungs, with more or less definite outlines, which are quite characteristic of metastases.

This usual picture is, of course, easy to recognize, but the most important element in the syndrome, however, is the scar of the operation or the history of the presence of the primary lesion. At times, however, the clinical picture of the secondary metastasis occurs so early in the course of the disease that it entirely masks the primary lesion as the following case indicates:

About a year ago a middle-aged woman was admitted on our medical service at the Lenox Hill Hospital complaining of severe pain, cyanosis, cough and expectoration. She had been treated about six months previous for heart disease, and for about four months before that for intractable neuritis of the left upper

extremity because of severe pains extending along the left arm and forearm. The examination showed the dyspnea to be due to fluid in both chests, which was more extensive on the right side. The left border of the heart extended to about five and a half inches to the left of the median line, but there was no evidence of any lesion of the heart. The most striking point in the examination, however, was the presence of a small adherent nodule, about the size of a walnut, in the left breast, with large adherent nodes in the left axilla. Upon exploring the left chest with the needle the fluid was found to be bloody in character. The pathology in this case was therefore very apparent. The so-called neuritis was due to secondary metastatic nodes in the left axilla from a primary carcinoma of the breast. The dyspnea, cyanosis and pleural effusion were all the result of the lung metastases, and these signs resembling the classic picture of myocardial insufficiency, assumed the important role in the syndrome. We corroborated our clinical ideas by roentgenographic examination and when the patient died a few weeks after admission, by an autopsy.

Primary lung tumors are much less common than secondary ones. The tumors may be benign or malignant. We can dismiss the benign tumors of the lungs with a few words as most of them are only discovered at the autopsy table and they give no clinical manifestations whatever. Dermoid cysts, however, merit more attention because these are the only benign tumors that may give clinical manifestations. They usually occur in the mediastinum, behind the sternum, and may exist there for years without any clinical disturbance. When, however, the tumor grows in size the only evidence is that of pressure in the mediastinum: dyspnea, cyanosis, cough and expectoration, or symptoms of pressure on the sympathetic nerves, such as pupillary changes. A definite diagnosis can only be made when the tumor finally ulcerates into a bronchus and hair or sebaceous contents of the cyst are expectorated. A dermoid cyst in the thorax may also be suspected when, after years of constant observation, the mediastinal tumor may be shown to be present without making any progress. Recently we have had under observation a patient who had a cyst about the size of a child's head in the right thorax which evidently came from the diaphragm and grew so rapidly that it occupied the lower half of the chest, displacing the lung upward. This mass gave the signs of consolidation which persisted for months and which showed in the roentgenographic shadow with a well-defined outline. There was no evidence of free fluid in the pleural cavity and the diagnosis of a tumor was readily made, principally on the basis of the roentgenogram and just as readily removed:

The most common type of primary lung tumors are the malignant ones. In spite of the fact that they are considered to be comparatively uncommon, we believe they are much more frequent than

we are in the habit of regarding them. The infrequency of these lesions is based upon autopsy statistics. Autopsy findings do not tell the whole truth, for the statistics are only of relative value. It is surprising to know that Dr. Sidney Yankauer in an extensive series of bronchoscopic examinations found that 12 per cent. of his cases had primary malignant tumors of the lungs, most of which were unsuspected. Pathologically, malignant tumors are of three types: carcinoma, sarcoma and endothelioma. The latter type of tumor is considered as a form of carcinoma or as an intermediate type between sarcoma and carcinoma. The carcinomata originate either at the pleural surface or at the hilus of the lungs; sarcomata usually begin at the hilus, while endotheliomata, which are very slow growing tumors, originate on the surface of the lungs. From the clinical standpoint the primary origin of the tumor is of great importance for the diagnosis of primary lung tumors, for the diagnosis must be made early and the primary location recognized. We therefore distinguish two clinical types of primary lung tumors: (*a*) Those that originate at the pleural surface, and (*b*) tumors that originate at the hilus of the lung and usually from a bronchus.

The early diagnosis of a primary lung tumor, which is the only useful diagnosis in these days of progressive thoracic surgery, cannot be made on one examination alone. The case must be studied for weeks or months at a time, as the progress of the case while under observation is of diagnostic importance. Besides, these tumors usually grow very slowly. The symptoms may be classified into three groups: (1) General symptoms; (2) symptoms of the pleural type; (3) symptoms of the hilus type.

The patient in whom we have a right to suspect a lung tumor usually comes to the physician complaining of cough, pain in the chest and dyspnea of long duration. It is quite evident that this syndrome does not suggest any definite lesion. These symptoms may be due to subacute bronchitis, pulmonary tuberculosis, cardiorenal disease or primary lung tumor, and with close study of these generic symptoms we may verify our supposition regarding this possible lesion. The cough is usually dry in the pleural type, while in the hilus type it may be accompanied by profuse, thick, purulent sputum and only occasionally by blood-tinged sputum. It is rare indeed to see the prune-juice sputum as described in text-books. The pain may resemble that of pleurisy or it may be substernal or supraclavicular. It does not necessarily have any relation to the primary site of the lesion. The dyspnea is a very important sign. Persistent and marked dyspnea, with a disproportion between the dyspnea and the physical signs, is an extremely suggestive sign of lung tumor. The patient may be suffering for months from cough, pain, dyspnea and expectoration, and these may be the only persistent physical signs with a small area of localized bronchitis and an inordinate amount of dyspnea. In such a patient, after we have

eliminated tuberculosis by repeated and thorough physical examination, by repeated sputum examinations, by tuberculin tests and by a complement-fixation test for tuberculosis we must then make all efforts to eliminate a primary lung tumor.

The physical signs are the characteristics by which we may be able to differentiate the type of the tumor. The signs of the peripheral type are largely pleural. Occasionally there is a friction rub, but the most characteristic sign is the occurrence of one-sided pleural effusion. The size of the effusion is not an indication of the size of the primary tumor. I have seen a small mass, the size of a walnut, give repeated pleural effusions of 2000 c.c. The effusion is invariably one-sided and the character of the fluid may be hemorrhagic, but it need not necessarily be so. Only about 50 per cent. of pleural effusions produced by primary lung tumors are hemorrhagic in character. As a rule it is serous in type, with the characteristics of a transudate. Occasionally on centrifuging the fluid we may obtain the characteristic large, highly granular cells which are believed to be pathognomonic of lung tumors, but we have rarely been successful in finding them except in one case in which the diagnosis was made without them. Recently the technic devised by Dr. Mandlebaum of Mount Sinai Hospital has made it easier to find these cells in the centrifuged fluid as well as in the sputum. Dr. Mandlebaum's method consists in embedding the centrifuged material in paraffin and then making serial sections. We have seen a chylous effusion in a case of primary lung tumor originating at the left apex of the lung, which was probably due to pressure on the thoracic duct. Of course, a pleural effusion may be just as suggestive of pulmonary tuberculosis, but the frequent recurrence of the fluid on the same side, especially when tuberculosis has been eliminated and when the fluid is bloody in character, is particularly suggestive of lung tumor.

Even when the pleural effusion is not present we may be able to diagnose a primary lung tumor by the localized bronchitis, with pain and inordinate dyspnea. When the tumor is large enough we may be able to make out a small area of consolidation on physical examination. Of course, if the case is followed long enough we may get all the signs of metastases: enlargement of the mediastinal area of dulness, glands, cachexia, etc., but the patient is then beyond therapeutic aid.

The hilus type is much more common and presents an entirely different picture. The patient suffers for weeks or months from what seems to be chronic bronchitis, and usually tuberculosis can be definitely ruled out. The sputum may be mucoid or purulent and only later does it become prune-juice in color. If the tumor begins near a bronchus the findings may be only those of a localized bronchitis, with consolidation later on. Usually in the hilus type the signs are those of severe dyspnea, with signs of compression of

a large bronchus, such as diminished breathing on auscultatory percussion and later on actual dulness and diminished breathing. It would seem, however, from the study of pathologic specimens of primary lung tumors, that we should get signs of massive consolidation. This is masked by the fluid, and when the fluid is removed we may get the signs of consolidation. But when these signs are present there is usually no diagnostic difficulty.

The hilus type of primary malignant tumor grows much more rapidly than the pleural type. The proximity of the tumor to the mediastinum is the reason for the occurrence, very early in the disease of pressure symptoms and metastases. The most common pressure symptoms are those of recurrent laryngeal paralysis, a one-sided dilated pupil from paresis, and finally paralysis of the sympathetic nerves; dilated veins over the sternum and local edema of the infraclavicular region; palpable left supraclavicular lymph nodes and finally enlarged axillary nodes, and increased areas of mediastinal dulness with myocardial insufficiency from pressure. Cachexia, which is a classic characteristic of the mediastinal type of malignant tumors and of malignant growths in other parts of the body, is absent in primary lung tumors until very late in the disease, and this symptom is therefore of little value for an early diagnosis.

The examination of the chest fluid holds out a helping hand, but unfortunately the grasp is not a very tight one. When we are most in need of aid it is usually of no value. When the diagnosis is evident these examinations are of corroborative help.

The characteristics of a typical specimen are only present in those cases with extensive involvement of the lung or of a hilus type which has perforated into the lumen of a bronchus. At first the sputum is not characteristic, but later on it may be found tinged with blood and still later it may resemble prune-juice, which is not due to the presence of blood and occasionally it has a characteristic greenish hue. Rarely we may find on microscopic examination proof of the tumor itself. Large polyhedral granules with faint vacuoles are believed to be almost pathognomonic, but they are rarely found when most needed. Centrifuging the fluid may bring out the characteristic granular cells, but this is rather a rare find. Dr. Mandlebaum, of Mount Sinai Hospital, has been able to find these cells more frequently by embedding centrifuged specimens in paraffin and making sections of them. It must be remembered, however, that sputum examinations are not of very great value. The finding of a few characteristic cells may be just enough diagnostic evidence to tip the scales in favor of a primary lung tumor. The diagnosis of a pleural effusion is usually not of great value. A hemorrhagic effusion is only indirect evidence of a malignant mass. Occasionally the lung puncture and examination of the aspirated material may show the tumor cells.

The nature of the tumor can only be surmised. The pleural type is more likely to be endothelial and then carcinomatous, while of the hilus type the most common tumor is usually sarcoma and less frequently carcinoma.

Examination of pathologic specimens of primary lung tumors seem to indicate that these masses show definite shadows on roentgenographic examination. Extensive involvement of the lungs by malignant tumor certainly does show very interesting pictures. But the condition is then quite advanced and the roentgenographic evidence is then merely corroborative. In early cases the roentgenogram does not show the definite evidence that we usually lack and that we are inclined to expect. The roentgenographic shadows of the lungs showing the primary lung tumors occur very late. We have watched two cases over a year before the roentgenogram showed a definite shadow in the lung. A mass in the mediastinum shows much more clearly and earlier than one in the pleura. Consequently when these shadows occur it is difficult to ascertain the primary lesion by study of the roentgenographic pictures. We had a man under observation about two years ago who gave a definite picture of primary lung tumor with metastases. The roentgenogram showed the mass in the mediastinum but no mass in the lung. Seven or eight plates were taken but none showed the mass in the lung, which we believed to be the primary tumor. At postmortem examination it was shown that we were correct in assuming the primary lesion to be in the lung and the secondary metastasis in the mediastinum, although the mediastinal shadows showed much earlier and more definitely than those in the lung. The recent method of roentgenographic examination after inflation with oxygen, devised by Drs. Stewart and Stein, is exceedingly helpful, in the roentgenographic study of primary lung tumor. By this method we may show masses in the lung much earlier than by the ordinary method. A case recently under our observation illustrates the advantage of this method. The patient had several pleural effusions in the chest in the course of a year and a half, several of which were bloody. Fourteen roentgenograms showed normal lung markings. We finally inflated the chest with oxygen after removing the fluid and the roentgenogram showed a definite mass about the size of a walnut at the right base on the pleural surface, which was corroborated at operation. We believe this was one of the first cases in which this method was used for the determination of a primary lung tumor. The mass was verified at operation and a lobectomy of the lung was successfully performed.

In the hilus type of tumor bronchoscopic examination is of distinct value. We believe in cases in which primary lung lesion is suggestive a bronchoscopic examination should always be done. In competent hands this method gives more evidence than any other and is practically devoid of danger. Even in cases of chronic

bronchitis where tuberculosis can be ruled out we believe bronchoscopy is indicated.

The value of bronchoscopy was never brought out so forcibly as several years ago, in a patient, on the surgical service at the Lenox Hill Hospital, who suffered apparently from bronchiectasis, for which she was operated upon a number of times in the course of two or three years. She would have periodic attacks of coughing, with profuse expectoration. Repeated operations during her stay in the hospital were without avail.

When she died an autopsy revealed a pedunculated benign adenoma which acted like a ball valve, causing interrupted obstruction of the bronchial tree, with retention of secretion. When the secretion had accumulated an attack was brought on and the coughing kept up until the fluid was expectorated, with relief of the symptoms for a few days. The mass found at autopsy could readily have been seen and just as readily removed through the bronchoscope.

The definite diagnosis of primary lung tumor depends upon the clinical findings. When the principal findings are those of mediastinal symptoms and a mediastinal mass the differential diagnosis is between different types of mediastinal tumors, mediastinal Hodgkin's disease and aortic aneurysm. The differential diagnosis between other types of mediastinal tumors and Hodgkin's disease cannot be made on any difference in the clinical features in the lungs. Mediastinal Hodgkin's disease can only be recognized by the presence of other glandular enlargements and the characteristic blood picture and morphological picture of a removed gland. Aortic aneurysm can be differentiated by the clinical picture, the positive Wassermann and the pulsating mass on fluoroscopic examination.

In the pleural type and in the type where there is no evidence of a mediastinal mass the difference lies between a tumor and pulmonary tuberculosis. Pulmonary tuberculosis can be ruled out by careful and repeated negative sputum examinations, by the absence of cachexia, by the negative tuberculin reaction, by the negative complement-fixation test and by the finding of a tuberculous lesion. Tuberculosis usually occurs in the upper part of the lung and travels downward, while primary lung tumors are much more liable to begin at the base of the lung. Fever and night-sweats may occur in both conditions with equal frequency. Not infrequently a primary lung tumor begins with evidence of primary infection, as the following case indicates. A young woman, aged about thirty-six years, was admitted to our medical service of the Lenox Hill Hospital with a lobar pneumonia. She had been ill for several weeks with a condition that began with sharp pain in the right side of the chest, dyspnea, high temperature which ran the course of a classic lobar pneumonia with consolidation. But the temperature never subsided nor did the consolidation ever clear up.

Repeated examinations of the sputum and complement-fixation tests for tuberculosis gave no evidence of tuberculosis. Repeated chest punctures gave no signs of fluid. Finally after about five or six weeks' observation with persistent temperature and apparently an unresolved pneumonia we obtained a clear serous fluid from the right chest, and we began to be suspicious that the lesion was a lung tumor. On taking a very careful history again it was brought out that about two years before the patient had a small nodule, the size of a walnut, removed from the left breast. We communicated with the surgeon who operated upon her and the pathologist who examined the mass and were told the mass proved to be a benign tumor. In a few weeks skin metastases and liver, abdominal and general metastases occurred, and the etiology of the condition was clear. The so-called pneumonia was evidently a pulmonary metastasis from a malignant tumor of the breast.

In spite of the apparently clear distinction between pulmonary tuberculosis and primary lung tumor the diagnosis of an early primary lung tumor is extremely difficult to make, and in doubtful cases an exploratory thoracotomy should be done. The tumor is then within the scope of modern surgery, and if the tumor proves to be a pleural one it can rapidly be removed with success.

The following case will illustrate the difficulty of differential diagnosis:

A man, aged about fifty-five years, was admitted to our service at the Lenox Hill Hospital with a one-sided pleural effusion which was of a serous character. Tuberculosis was definitely ruled out by repeated negative sputum examinations, by repeated negative tuberculin tests, by negative physical signs and numerous examinations and by negative complement-fixation test. We observed this man for about a year and a half, examining him repeatedly for tuberculosis and primary lung tumor. About fourteen roentgenograms were taken in the course of a year, all of which were negative, although he was aspirated a number of times, only two pleural effusions were bloody in character. After careful study we made the diagnosis of a primary malignant tumor of the lung which we finally demonstrated after oxygen inflation by the Stein and Stewart method to be about the size of a walnut. An exploratory thoracotomy showed the mass at the base just as we had proved clinically. It seemed to be a malignant tumor the size of a walnut and a lobectomy of the lower lobe of the right lung was done by Dr. Franz Torek. The patient made a stormy recovery and finally died about seven months later of chronic nephritis. The tumor turned out to be a cartilaginous tuberculous mass.

Conclusion.—The diagnosis of a primary lung tumor is one of the most difficult pulmonary lesions to recognize early. This can only be done with a fair degree of certainty. If we wait until we can do so positively the patient is beyond our therapeutic reach. Conse-

quently when the condition cannot be recognized definitely an exploratory thoracotomy should be performed whenever there is a reasonable suspicion of a primary tumor of the lung. If such a lesion is present it can be removed at the time when the operative risk is at a minimum and the chances for recovery are at their height.

Clinically we may recognize two distinct types of primary lung tumor, the pleural and the hilus type. The pleural type is most amenable to surgical treatment.

A reasonable suspicion of the presence of the pleural type of primary lung tumor is based upon the occurrence of a one-sided pleural effusion, with or without bloody fluid, in the absence of definite signs of tuberculosis. The roentgenograms of the chest taken when the pleural cavity is inflated after removing the fluid is one of the best methods to demonstrate the mass in the lungs.

The hilus type is not so amenable to treatment, and the most important indications of its presence are the persistence of chronic bronchitis in the absence of tuberculosis, with evidence of blood-tinged sputum and the subsequent evidence of a mediastinal mass with pressure symptoms. In these cases bronchoscopic examination is of the greatest diagnostic value and gives the earliest evidence.

Finally, I believe that careful study of many cases of recurrent pleurisy and chronic bronchitis will reveal that primary lung tumors are much more common than we have heretofore believed.

INTUBATION AND VISUALIZATION OF THE DUODENUM IN SUSPECTED LESIONS OF THE PYLORUS, DUODENUM, AND GALL-BLADDER.

By I. O. Palefski, M.D.,
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The technic and the diagnostic significance of this procedure were described previously.[1] Its purpose is to determine whether defective filling and distortion at pylorus and the first part of the duodenum, is due to ulcer, pericholecystic adhesions, pressure from neighboring organs or caused reflexly from the intestines or other abdominal organs. From the writings of Smithies,[2] Carman[3] and Cole[4] it appears that this differentiation is not always possible. The experience of Lockwood is of interest. He states:[5] "Over four-fifths of duodenal ulcers that I have seen

[1] Jour. Am. Med. Assn., December 4, 1920. Med. Rec., April 18, 1914.
[2] Jour. Am. Med. Assn., November 30, 1918. [3] Ibid., March 28, 1914.
[4] Lancet, May 2, 1914.
[5] New York State Med. Jour., December, 1917.

diagnosed by the roentgen ray have turned out nothing more than chronic appendicitis. The picture may be perfect, the photograph may be clear-cut; but the diagnosis derived from inference of disturbed gastric function and distortions of the cap may be alto-

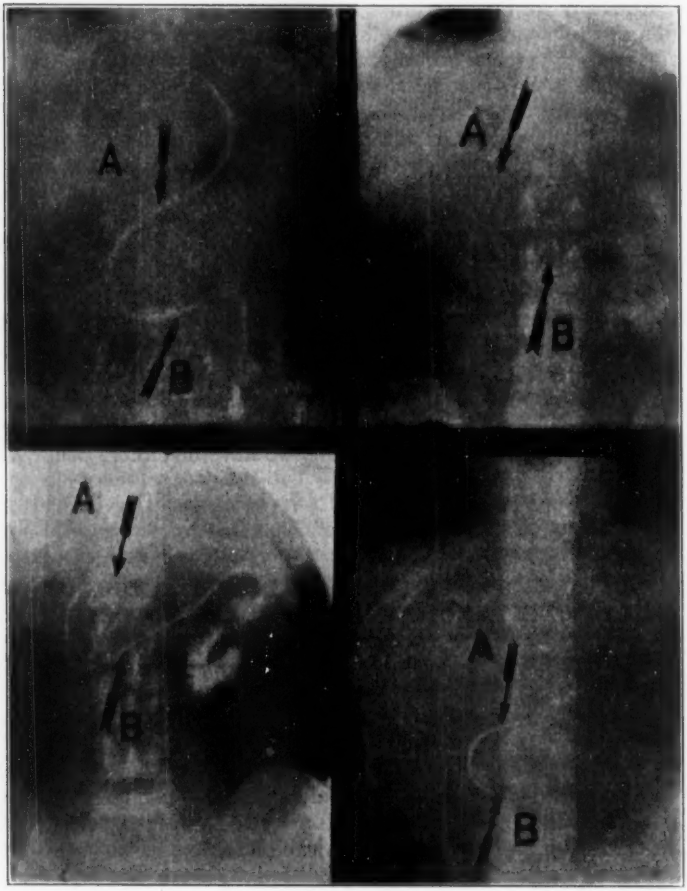

FIG. 1.—Curve of the duodenal tube in the normal duodenum. *A*, lesser curvature; *B*, duodenum and jejunum; normal distance between *A* and *B* is 7 to 9 cm.

gether valueless. My remarks are suggested by the results obtained from a variety of sources." Indeed, it appears to me that many of these roentgen-ray errors are preventable by using the fluoroscope, by making more exposures and by repeating examinations. It must be conceded that in a large number of cases the roentgen-ray

diagnosis of lesions about the pylorus, duodenum and gall-bladder is not corroborated even when made by a skilful roentgenologist. Experience has shown that defective filling, distortion, spasm and altered gastric evacuation are no more characteristic of duodenal ulcer than of periduodenal cholecystic adhesions and that the latter is usually taken by the roentgenologist for the former. Employing both clinical and roentgen methods, I have learned to depend chiefly upon roentgen-ray findings in gastric lesions and upon intubation and visualization of the duodenum in duodenal ulcer and gall-bladder disease.

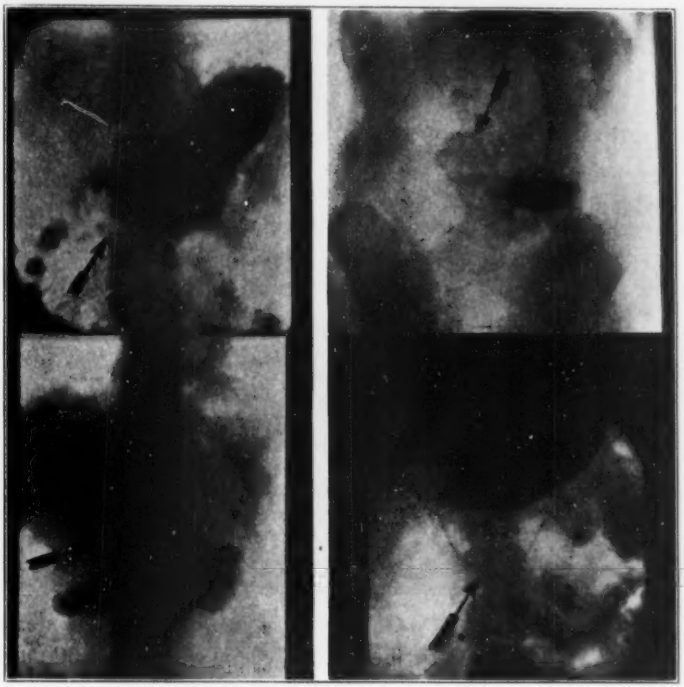

FIG. 2.—Variations in the curve of the duodenal tube in the normal duodenum in four patients. (Note arrows.)

Duodenal intubation and visualization is a clinico-roentgen procedure of twofold purpose: (1) The examination of duodenal juice for its physical, chemical, microscopical and bacteriological properties; a change in the normal color and transparency; the persistent presence of blood in any form; an increased amount of mucin and number of epithelial cells and bacteria in duodenal juice signify infection and inflammation situated in the duodenum, biliary ducts

or gall-bladder. (2) A roentgen study is made of the course the duodenal tube assumes from the stomach to the jejunum. In stomachs of normal size and position it forms a horseshoe curve; the tubing in the third part of the duodenum is about 7 to 9 cm. below that running along the lesser curvature (Figs. 1, 2, 4 and 6); in peripyloric and periduodenal cholecystic adhesions this position is altered. The tube then appears either twisted, kinked or angulated (Figs. 8, 10, 11 and 12). Ordinarily these adhesions may escape detection or show roentgen signs indistinguishable from duodenal ulcer.

FIG. 3.—Double filling defect of the first part of the duodenum due to duodenal ulcer discovered shortly after appendectomy. Patient, H. F. Male, aged twenty-eight years. Referred by Dr. H. Finkelstein, N. Y., June, 1917. (See Fig. 4.)

The diagnostic significance of their presence lies in the fact, as emphasized by Smithies,[6] that these are usually associated with chronic cholecystitis. The detection of periduodenal adhesions, therefore, should arouse the suspicion of the presence of chronic gall-bladder disease.

The technic of this procedure is rather simple, although at times it may require two or three hours for its completion. My modified

[1] Loc. cit.

duodenal tube,[7] owing to its small size and heavy weight, is best adapted for this examination. It is introduced to the 20-inch mark and the patient is given a glass of cool water to drink and then assumes the right posture. In the absence of obstruction the tube passes into the duodenum in thirty minutes and with the patient in the Trendelenburg position, reaches the jejunum in about one hour or longer. Specimens of duodenal juice are aspirated at short intervals and then the tube is injected with a suspension of barium, one-half glass of which is also taken by mouth. Roentgen-ray

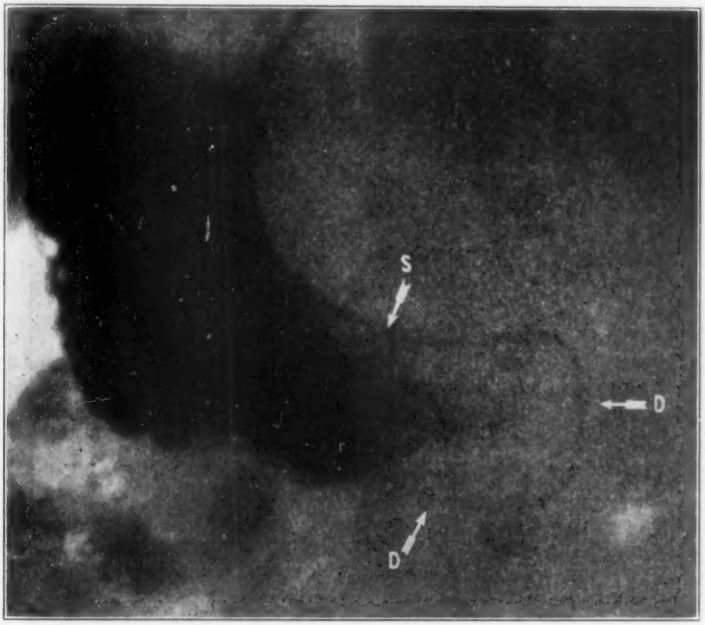

FIG. 4.—Patient, H. F. Note normal horseshoe curve of the duodenal tube in duodenal ulcer. Blood in the duodenal juice. Symptoms and filling defects disappeared since medical treatment, three years ago.

exposures are then made in the erect and prone, the latter being more diagnostic. Care must be taken to place the roentgen-ray tube at right angle to the patient and the latter flat against the screen holding the film. The duodenal tube is then slowly removed and cleansed. I have used this method in the following group of cases:

Prepyloric Ulcers and Adhesions. Ulcers situated at the antrum, not involving the lesser curvature, may either escape detection alto-

[7] Obtainable from the Kny-Scheerer Corporation, 56 West 23d St., New York.

gether or cause suspicion by only one or more minor roentgen signs, such as incisuræ or intensified gastric peristalsis. In a number of patients these ulcers do not cause pronounced symptoms, except gastric distress, distention and eructation. On the other hand, peripyloric cholecystic adhesions may produce marked gastric distortion simulating typical penetrating gastric ulcer when surgical interference is urgently advised. The duodenal tube is of diagnostic

FIG. 5.—Defective filling of the duodenum in chronic appendicitis. Patient, R. S. Female, aged twenty-two years, referred by Dr. M. Schmerzler, Brooklyn, January, 1919. Exploratory laparatomy by Dr. H. Haubold, Harlem Hospital, New York. (See Fig. 6.)

aid in this group of cases. Its passage into the duodenum is delayed or prevented, owing to pylorospasm. Specimens of gastric contents aspirated at frequent intervals may show occult blood in the ulcer. In adhesions the distorted curve of the duodenal tube is readily observed.

Duodenal Ulcer. Many a patient suffering from duodenal ulcer is regarded as neurasthenic on the strength of negative roentgen-ray findings. I have seen instances in which fairly large callous ulcers

of the cap showed no roentgen evidence whatsoever. On the other hand, defective filling of the duodenum, in my experience, is less frequently due to duodenal ulcer, as is generally supposed, than to periduodenal cholecystic adhesions. A case with gastric symptoms showing high gastric acidity one hour after an Ewald meal, delayed gastric evacuation after a mixed meal, blood in duodenal contents and a normal horseshoe course of the duodenal tube may safely be regarded as duodenal ulcer whether or not there is

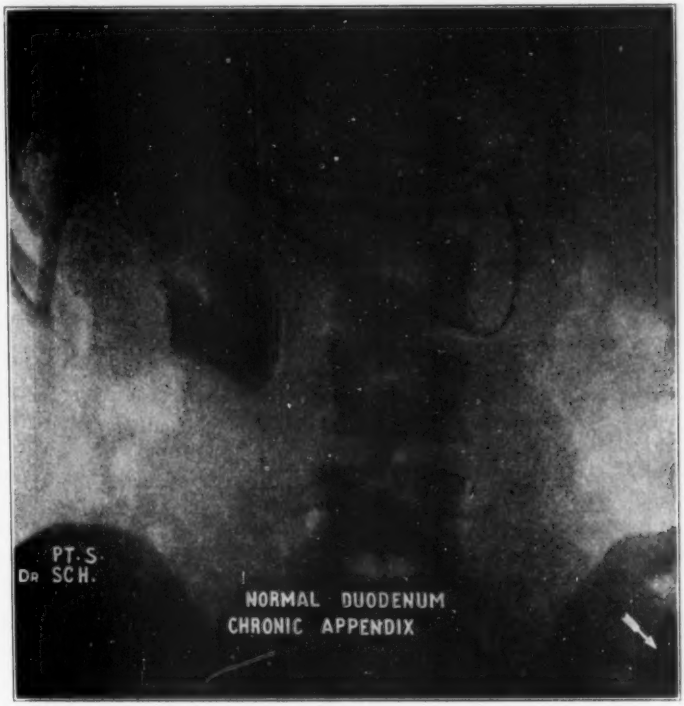

FIG. 6.—Patient, R. S. Note normal horseshoe curve of the duodenal tube. Visualized appendix. (See arrow.)

defective filling of the duodenum. It may be of interest to recall, at this junction, the emphasis by Rehfuss[8] of the frequent presence of bile, and blood in duodenal ulcer, in specimen of gastric contents obtained by the fractional method "at the phase of tryptic regurgitation" I found this, by roentgen-ray observation, to be due to the passing of the metallic end of the tube beyond the pylorus.

[8] Jour. Am. Med. Assn., November 9, 1918.

The specimen is thus aspirated directly from the duodenum. It should be remembered that the tests, except the roentgen ray and the fluoroscope, for the localization of the tube, are not always dependable.

Chronic Cholecystitis with Periduodenal Cholecystic Adhesions. This group includes a large number of cases presenting a chain of symptoms simulating either ulcer, chronic appendicitis, intestinal stasis, neurasthenia or, in the female, pelvic disturbances. In

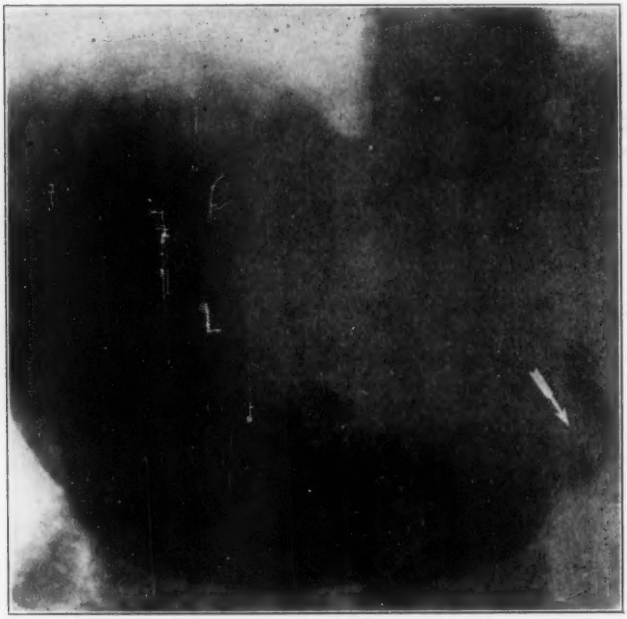

FIG. 7.—Defective filling of the duodenum in chronic cholecystitis, with periduodenal cholecystic adhesions simulating duodenal ulcer. Patient, M. G. Male, aged forty-one, referred by Dr. M. Weitzen, N. Y., June, 1917. Exploratory laparotomy by Dr. William H. Luckett, Harlem Hospital, N. Y. (See Fig. 8.)

many of these there is also roentgen evidence of duodenal ulcer. It is often a surprise to the clinician and surgeon when on exploratory laparotomy no ulcer is found, but instead a thickened gallbladder and periduodenal cholecystic adhesions. These cases can now readily be recognized by duodenal intubation and visualization. A case with gastric symptoms showing tenderness in the right hypochondrium, normal or subnormal gastric acidity, delayed gastric evacuation after a mixed meal, a distorted course of the duodenal tube with or without defective filling of the cap may safely

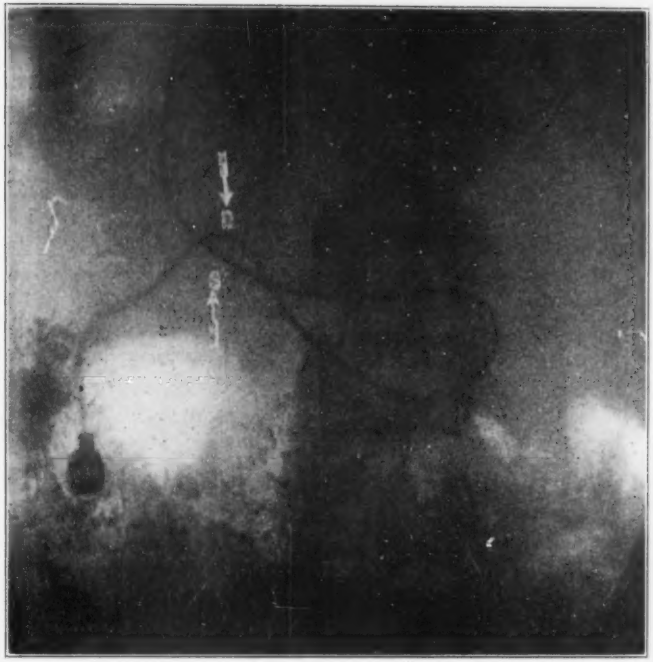

FIG. 8.—Patient, M. G. Note deflected course of the duodenal tube in periduodenal cholecystic adhesions. The tube in the third part of the duodenum is above that at the lesser curvature. (See arrows *D* and *S*.)

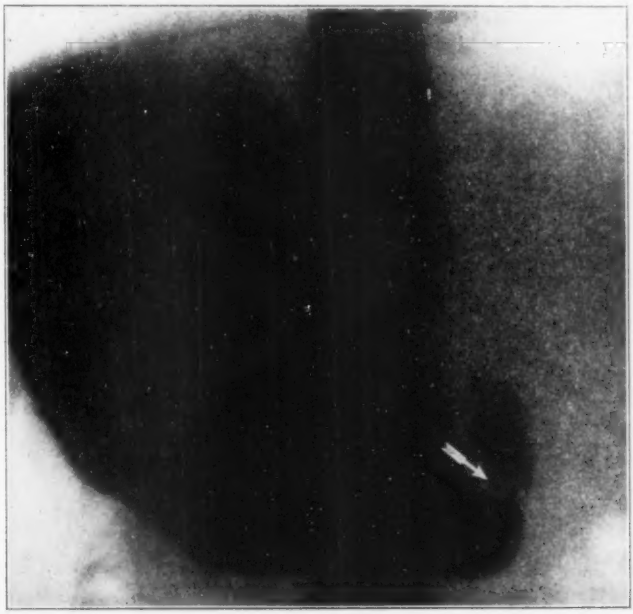

FIG. 9.—Normal pylorus and duodenum in periduodenal cholecystic adhesions. Patient, S. R. Female, aged twenty-two years. Exploratory laparotomy by Dr. William H. Luckett, June, 1917. (See Fig. 10.)

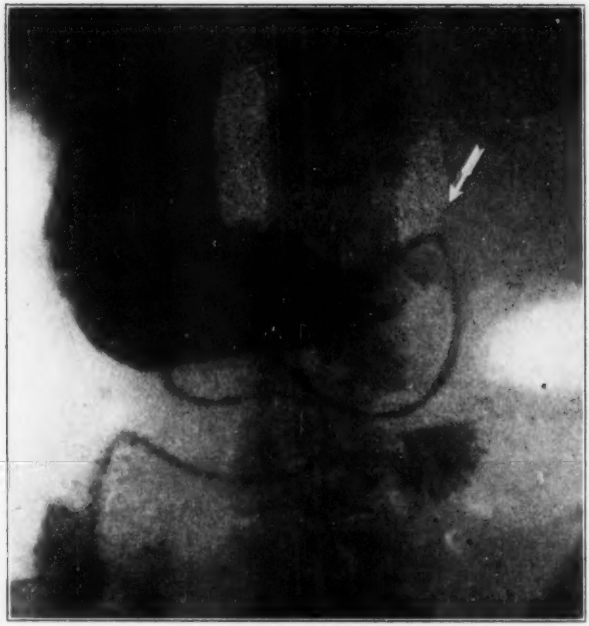

FIG. 10.—Patient, S. R. Note angulation of the duodenal tube in the duodenum due to periduodenal cholecystic adhesions. (See arrow.)

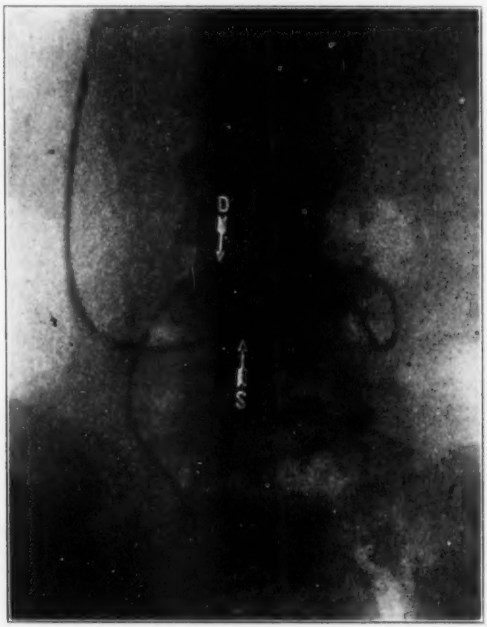

FIG. 11.—Perigastric periduodenal adhesions. Patient, R. F. Exploratory laparotomy by Dr. William H. Luckett, Harlem Hospital. Note twisted course of tube. The duodenum (*D*) is above the lesser curvature (*S*).

FIG. 12.—Postoperative periduodenal cholecystic adhesions causing biliary colic and jaundice. Patient, R. Female, aged forty-eight years. Exploratory laparotomy by Dr. C. Goodman, Beth Israel Hospital, N. Y. Note twisting of the tube in the second part of the duodenum, the latter being internal to the first part. (See arrows.)

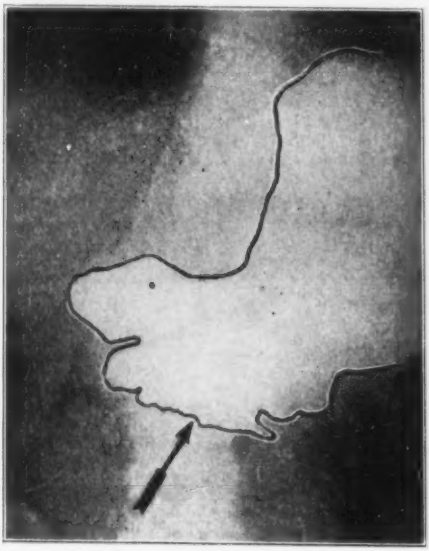

FIG. 13.—Jejunal obstruction following gastro-enterostomy caused by perijejunal adhesions. Patient, S. G. Female, aged thirty-one years. Exploratory laparotomy by Dr. C. Goodman, Montefiore Home and Hospital. (See Fig. 14.)

FIG. 14.—Patient, S. G. Note twisted curve of duodenal tube.

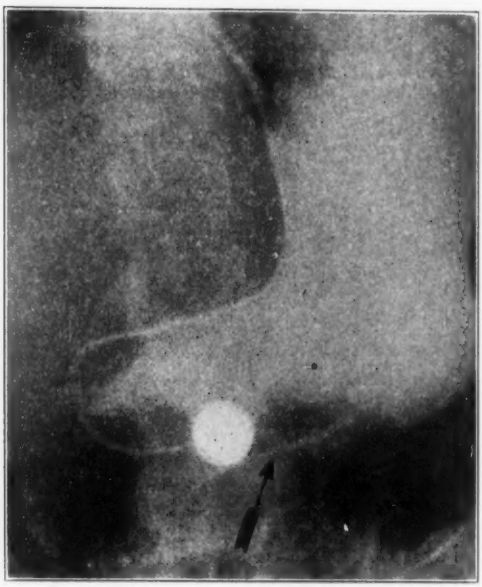

FIG. 15.—Patient, S. G. Note normal course of the tube in the jejunum after separation of the adhesions.

be regarded as chronic cholecystic adhesions (Figs. 6, 7, 8, 9). Most of these cases also show gastric hypermotility six hours after a barium-zoolak meal, turbidity, increased mucin, epithelial cells and bacteria in the duodenal juice. There is usually a history of constipation.

Postoperative Adhesions. Duodenal intubation and visualization offer a practical method of detecting postoperative adhesions after surgery upon the stomach and gall-bladder. In some cases adhesions do not evidently cause pronounced symptoms, while in others the symptoms are suggestive of interference with the patency of the common bile duct or with gastric evacuation (Figs. 12, 13, 14 and 15). In recurrent symptoms after gastro-enterostomy the duodenal-tube is allowed to pass through the anastomosis and outline the jejunum. In perijejunal adhesions the course of the tube in the jejunum is twisted (Figs. 13 and 14).

The conclusions drawn in this paper are based upon an experience of several years on a considerable number of patients, including about 400 established cases. It is not intended that this method should distract from the diagnostic value of the older and well-established methods, but when combined with them at least 90 per cent. of duodenal ulcers and no less than 75 per cent. of gall-bladder disease should be detected even in their incipiency. I must emphasize, however, the importance of proper technic.

THE TREATMENT OF EMPYEMA WITH GENTIAN VIOLET.

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Our conceptions of the etiology, pathology and treatment of empyema have undergone a marked change as the result of observations made during the past two years. It may be a question whether our influenza experience has brought out striking advances in the therapy of that disease, but there can be no doubt that in the treatment of postinfluenzal empyema we have made tremendous strides. Whether these lessons learned in the treatment of postinfluenzal empyema are applicable to other forms of empyema the future must decide.

The treatment of empyema following influenza by the older orthodox surgical methods was followed by such an appalling mortality that many felt we were dealing with a disease quite different from the conventional postpneumonic empyema of the past. Also, postinfluenzal empyema is a complication of bronchopneumonia

and presents many differences when contrasted with an empyema following lobar pneumonia, from which we have gained most of our knowledge of empyema in the past. Moschcowitz,[11] however, pointed out that empyema in the past was not a benign condition, the figures at Mt. Sinai Hospital in New York from 1904 to 1914 showing a mortality of 28 per cent. He collected further statistics which show that the death-rate in empyema before the two great influenza epidemics varied from 18.9 per cent (Lilienthal) to 55 per cent (Lavrow). This high mortality was not generally appreciated, however, until empyema was seen *en masse* in the great army hospitals during the past two years as a complication of influenzal bronchopneumonia. The marked fall in the death-rate which followed the policy of delaying operation and of carrying out first a series of preliminary aspirations suggest the interesting query whether these newer methods of treatment would have lowered the empyema mortality in the past.

During the past winter a large number of persons suffering from influenza were treated at the Henry Ford Hospital, where many of these patients developed empyema. It is the purpose of this report to discuss the results obtained in treating these empyema cases, and particularly a group treated by repeated aspirations and intrapleural instillations of gentian violet.

Many differences of opinion prevail regarding the cases to be considered as empyema. Hartwell[7] in his discussion of empyema uses the term to indicate "a purulent exudate within the general pleural space." "Local collections of pus," he states, "walled off by adhesions are intrapleural abscesses or interlobar abscesses," and as such he excludes them from his discussion. Moschcowitz (*l. c.*), on the other hand, states that "nearly every empyema is an encapsulated one." Aside from these differences in opinion based upon anatomical considerations there are differences in terminology dependent upon the character of the pleural effusion, many observers limiting the term empyema to cases yielding only frank macroscopic pus. Graham,[4] however, in his summary of reports from the various Base Hospitals notes that the exudate most commonly found is a slightly turbid serofibrinous fluid. In our group of cases all patients showing a turbid pleural fluid containing microörganisms are classed as empyema, the fluid in question varying from a slightly turbid serofibinous exudate to a thick, creamy pus.

Objection may be raised to the inclusion in our discussion of certain cases as postinfluenzal empyema, on the ground that they were simply cases of streptococcus pneumonia complicated by streptococcus empyema. As certain of these cases were not observed until after the onset of the empyema, and as the symptoms of influenza show much variation, this objection has some weight. On the other hand these cases of empyema occurred during the height of the influenza epidemic, presented a similar clinical picture, ran the

same clinical course and had bacteriological findings identical with those cases of influenza observed from their onset. Because of this similarity and the lack of definite evidence to the contrary all the cases of empyema occurring during this epidemic have been considered as a single group. Also it must be emphasized that at the present time we have no definite criteria, either clinical or pathological, by which postinfluenzal streptococcic empyema can be differentiated from empyema following a primary streptococcus bronchopneumonia occurring during an influenza epidemic, or in fact from an empyema complicating a measles bronchopneumonia.

The study of our series of cases, although small, brings out some points of interest. In all there were admitted to the hospital 312 cases with the clinical diagnosis of influenza; 40 of these cases, or 12.5 per cent, developed empyema, and of these 17 died, a mortality of 42.5 per cent. This mortality is higher than that reported in a summary of 25 army camps collected by Graham, which was 30.2 per cent, but not so high as that reported from some of the Base Hospitals—for instance, Camp Funston with 84 per cent and Camp Wheeler with 65 per cent. These statistics, however, like many of those published, lose much of their value because of a failure to distinguish between the mortality of empyema and that due to bronchopneumonia. Graham (*l. c.*) has also pointed out that in the army statistics much of the discrepancy is due to differences in definition of the term empyema. In those camps in which the term empyema was limited to cases showing frank pus the mortality was the lowest, while in the camps including also cases of serofibrinous effusions the mortality was much higher. The latter classification was used in our series and doubtless accounts in great measure for the high mortality. The differentiation made by Graham agrees with the observations of many writers, and our cases also show that the serofibrinous exudation corresponds in time to the presence of an acute pneumonic process, and consequently the period in which most deaths occur.

The conclusion of Moschcowitz (*l. c.*) that when a patient dies with an empyema in the acute stage the cause of death is the pneumonia and not the empyema is shared by most observers. Fifteen of our 17 deaths occurred in the presence of an acute demonstrable pneumonia, 10 of them within one week after admission to the hospital. Eleven of the fatal cases showed a serofibrinous exudate, 6 showed frank pus. One of the latter, however, died from streptococcus peritonitis following ulceration of the bowel and one other patient was a case of neglected empyema admitted *in extremis*.

The disastrous experience following too hasty operative intervention in empyema was so uniformly noted in the influenza epidemic as to constitute the most important single observation made on this subject during the past two years. Rodman[14] noted in his work at Camp Bowie that the mortality was 45 per cent in the cases

in which the method of early operation was employed. Later, when he aspirated until frank pus appeared, the mortality dropped one-half. Stone[15] reported a mortality of 61.2 per cent in 85 patients operated upon immediately following the establishment of the diagnosis. Among 190 patients operated upon after a series of preliminary aspirations the mortality fell first to 12.6 per cent and a later series showed a still lower rate of 9.5 per cent. Following a series of such experiences reported from various parts of the country the method of preliminary aspiration rapidly became the method of choice, and its value was emphasized particularly in the report of the Empyema Commission[4] and in a more recent article by Moschcowitz (*l. c.*). A number of methods of closed drainage also made their appearance; the method of Mozingo,[10] irrigation with Dakin's solution through a trocar; the method of Phillips,[13] irrigation through a catheter, and the method of Harloe,[6] who inserted a catheter into the chest through which the pus was aspirated at various times, and which was clamped off during the intervals. Each of these three methods gave excellent results in the hands of their originators. A similar treatment was employed by Manson,[9] who treated a series of cases by repeated irrigation with chlorinated soda through a catheter. He treated 43 patients by this method; all were cured and no secondary operation was necessary. In discussing the excellent results obtained by many observers who employed first aspirations followed later by operation it must be emphasized that their low mortality was due partly at least to the fact that they were treating the more resistant patients of their series, the others having already succumbed to an acute bronchopneumonia.

Many scattered instances are reported in which the empyema cleared up under the preliminary aspirations and resort to operation became unnecessary. At the onset of our empyema experience repeated aspiration was performed on the patients with the object of preparing them for a subsequent operation. It was thought at the time that this preparation would be assisted by the use of some bland antiseptic solution capable of destroying bacteria without causing any marked irritation of the pleural surfaces. The solution used for this purpose was an aqueous solution of gentian violet, which has been shown by the investigations of Churchman[1 2 3] to possess a high bacterial value *in vitro* for most Gram-positive organisms, and also to have a value in the treatment of suppurative processes.

The procedure was as follows: The chest was aspirated by means of a Potain aspirating outfit, the fluid withdrawn and 100 c.c. of an aqueous solution of gentian violet introduced into the chest through the aspirating needle by means of a Luer syringe. This solution was allowed to remain until the next aspiration. At first a dilution of 1 to 10,000 was used, followed later by dilutions of 1 to 5000 and

1 to 1000. Later in the series the first instillations were used in the strength of 1 to 5000, followed rapidly by an increase in strength to 1 to 1000. As this method was followed in a number of the earlier cases by a sterilization of the pleural exudate and clearing up of the empyema the procedure was extended to all the cases coming under observation. The greater number of the cases cleared up under this treatment, there were some failures, and in a few instances it is now apparent that surgical intervention should have been resorted to earlier.

Twenty-seven cases in all were treated in this way. Of this number 14, or 51.8 per cent, were cured; 8, or 29.6 per cent, were not cured by this procedure but later came to operation; 5, or 18.5 per cent, died. Of the fatal cases 3 died of pneumonia present on admission and persisting during treatment, while 1 patient died of peritonitis having its origin in a diphtheritic enteritis with ulcer formation and perforation of the intestine. This mortality of 18.5 per cent, although admittedly high, is mostly a pneumonia rather than an empyema mortality, and compares favorably with the mortality statistics previously quoted and also with those of Ingraham,[8] who reports an operative mortality of 31.8 per cent, and of Gray,[6] whose mortality was 21 per cent.

The character of the fluid obtained in the successful group of cases varied. In 3 instances it was serofibrinous, 2 of these patients clearing up after two treatments and the third after six treatments. A fourth patient showing a similar fluid cleared up after two aspirations without the use of any gentian violet. This recovery was not included in the statistics for this reason. All of these showed a pure culture of Streptococcus hemolyticus in the pleural fluid. Another patient with bronchopneumonia developed a sterile serofibrinous effusion that disappeared with one aspiration, the case resembling one reported recently by McCrae,[12] who describes a turbid pleural effusion in a case of lobar pneumonia that cleared up following one aspiration.

In 6 of the 14 successful cases frank pus was obtained at the first aspiration and the fluid continued to be quite thick and purulent, later becoming thinner and finally disappearing altogether. This group is of considerable interest in showing that cases with frank pus do clear up following repeated aspiration and gentian violet instillations, and that rib resection with open drainage is not the only method whereby such cases can be cured.

In 5 of the cases the fluid was at first serofibrinous but later became markedly purulent and remained so until it cleared up. In all, 11 out of the 14 showed frank pus during the course of treatment, and belong to the group of undisputed empyema cases.

Bacteriological studies of the pleural fluid in the 27 cases treated by aspiration and gentian violet injections showed the hemolytic streptococcus present in pure culture in 17 cases; associated with the

B. influenzæ in 4; associated with the pneumococcus in 2; associated with both the pneumococcus and B. alkaligenes in 1; while in 1 instance the Streptococcus hemolyticus, pneumococcus and B. influenzæ were all found at various times in the fluid; in 2 of the cases the pneumococcus was grown in pure culture. In those cases showing more than one organism in the pleural fluid the bacteriological findings varied with different aspirations, one microörganism growing at one time, another at other times and often both together.

The number of treatments employed before recovery varied greatly. While in one instance only one treatment was necessary thirty-eight had to be employed in another case. The average has fourteen to sixteen. There was no appreciable difference between the number of treatments necessary in cases in which frank pus or where serofibrinous fluid was obtained at the first aspiration. These results are of interest in emphasizing that in all cases the fluid after a few aspirations became purulent and that the presence of a serofibrinous fluid indicated only that the patient had been aspirated at an earlier stage.

In the successful cases two noteworthy effects of treatment were observed: a gradual lowering of temperature and a diminution in the amount of fluid obtained at thoracentesis. While a decrease in the amount of fluid was usually a good sign, yet this alone without a lowering of temperature did not prognosticate a favorable outcome, as it occurred in a few patients who failed to clear up. This failure of the amount of fluid obtained at tapping to serve as a prognostic index is probably to be explained anatomically—a failure to drain the cavity thoroughly because of inaccessible pus pockets.

A study of the temperature curves in all of the successful cases showed that the treatments very soon reduced the fever. In some instances this fall was rapid and a normal temperature was reached in from two to seven days. Such a reduction was, however not the rule, and the average length of time before a normal temperature was reached was fifteen days, during which time the patients were treated from once a day to once in three or four days. In our experience those patients who were treated frequently, as often as every day in the beginning of the temperature, made, as a rule, the most rapid and satisfactory recoveries. In several instances the patients after a week or longer of normal temperature showed sudden rises of temperature which persisted for a few days but disappeared when treatment was resumed. Several patients also showed complications in the form of erysipelas and acute arthritis which complicated the picture of the temperature curve and undoubtedly extended the febrile stage.

In contrast to this fall of temperature in the successful cases the unsuccessful ones showed neither rapid nor gradual response to aspiration and gentian violet instillation. In most of these cases this treatment did not produce freedom from fever for a single day.

In one case there were occasionally remissions of one to two days followed by periods of fever lasting from one to two weeks. One other case showed marked reaction to tapping and fever-free periods of a week at times. This patient was later operated upon at his own request.

The absence of microörganisms in the pleural fluid was, of course, a favorable sign, but one which, as a rule, appeared late in the course of treatment. In many patients also the fluid was not wholly sterile at the time of the last aspiration, although the number of microörganisms was very greatly reduced. The leukocyte count, while it steadily fell as the patients responded to treatment, showed such great variations that it could not be used as a very reliable prognostic index.

The result of these observations indicates that definite response to the treatment should appear within two or three weeks of frequent treatments if this method is to result in recovery. If this response is absent, successful results with this treatment are doubtful and thoracotomy is indicated.

Moschowitz (*l. c.*) in discussing the pathology of empyema lays stress upon the presence of ruptured subpleural pulmonary abscesses and states that irrigation of empyema cavities with irritating solutions such as Dakin's solution results in coughing and choking. In our experience the presence of such communications between the bronchus and the pleural cavity was strikingly shown by the appearance of a violet-stained sputum in 19 of the 27 cases treated. In the first cases noted the question was raised whether the appearance of the dye-stuff in the sputum was not due to penetration of the lung by the aspirating needle. While this possibility cannot be absolutely ruled out, further observation led to the conclusion that it was unlikely. In all aspirations extreme care was used not to penetrate the lung itself; the appearance of the dye-stuff in several cases was instantaneous upon introduction of the gentian violet into the pleural cavity; also in other patients the dye-stuff was coughed up suddenly several days after the intrathoracic injection. In another group of patients the frequent expectoration of thick pus led to the conclusion that a bronchopleural fistula was present.

The duration of the patient's stay in the hospital after the development of empyema is a question that must be taken into consideration in the choice of a method of treatment. This question has not been studied in detail in many of the empyema reports doubtless because of the difficulty in tracing these cases which in the army camps were frequently transferred. Ingraham (*l. c.*) states that the average stay of his cases in the hospital was 78 days—22 days before operation and 56 days following operation. Gray (*l. c.*) found the average number of days in the hospital to be 92 at Fort Des Moines. Tinker and Wattenberg[16] have reported in

their studies on the treatment of empyema some interesting figures. Their series comprise 80 cases—all but 6, however, were operated upon elsewhere and transferred to them for after-treatment. The average stay of the patients in their hands was only 34 days, but as the average length of suppuration before admission was four months their general average was over five months. One of their patients had been suppurating eleven months before coming into their hands and another was under treatment for five months before recovering.

The average stay in the hospital necessary for our cases, which were cured by aspiration and gentian violet instillation, was 76 days, the longest 120 days, the shortest 25 days. The average length of stay in the group unsuccessfully treated and later subjected to thoracotomy was 101 days, the longest 112 days and the shortest 92 days. The patients who were operated upon were discharged from the hospital on the average of 39 days after operation. This indicates that the previous treatment of the patient by aspiration and intrathoracic injection had not, as a rule, rendered the surgical problem more difficult nor delayed the time of recovery. In one conspicuous example a bilateral empyema by means of this treatment cleared up on one side, and the remaining empyema being limited to one side, proved a simple surgical problem. The average length of stay of all patients was 84 days, which compares favorably with the figures above mentioned. This period of time could doubtless have been somewhat shortened by an earlier operation in a few of the cases which failed to improve rapidly after treatment and and who in the light of our experience now should have been operated upon sooner. Our cases also were kept in the hospital on the average of a month with a normal temperature before discharge, a period which doubtless could be considerably shortened.

The cases in this series have been followed closely in order to ascertain the after-results of the treatment. One of the patients died subsequently after discharge from the hospital from what was apparently acute cholecystitis. This patient had responded very readily to treatment, and at the time of her discharge showed nothing abnormal in the chest but the presence of some pleural thickening. Nine of the patients returned to the hospital in response to recall letters and showed only the signs of a thickened pleura on the affected side. All of these persons are at work and consider themselves cured. The physical signs at present do not indicate an excessive pleural thickening and none of them show any recognizable deformity. Four other patients have been followed by letter and have made perfect recoveries. Letters from their physicians of 2 of these state that they have recovered entirely and show only slight signs of a thickened pleura. There have been no relapses. This point has been very carefully studied, and this report has been delayed largely because it was desired to allow a sufficient

time to elapse to be sure the patients were cured. It has now been over four months since the last patient was discharged from the hospital.

Summary. In a series of 27 cases of postinfluenzal empyema, 14, or 51.8 per cent, were cured without operation by repeated aspiration and intrapleural instillations of gentian violet. No relapses occurred and no deformities of the chest developed. The presence of frank pus was no contra-indication to treatment by this method. It is possible that some of these cases would have recovered without the use of gentian violet installations, yet because of the prompt symptomatic response to such injections and the rapid diminution or disappearance of bacteria in the pleural fluid it was evident that the dye-stuff possessed a very definite bactericidal value.

The most valuable indication that a patient is responding to treatment is a lowering of temperature immediately following aspiration, which persists and gradually reaches normal. A diminution of microörganisms or a frequent absence of them in the aspirated fluid is a favorable sign, but only when there is a temperature response to aspiration. Patients who failed to show such reactions to treatment in 15 to 20 days in our experience did not recover by this method. If the aspirations and instillations are not effectual within this time surgical intervention is indicated. This method of treatment should delay the operation only slightly longer than usual while making an attempt to clear up the empyema during this period. Failures were due usually to inability to empty the pus because of extensive pocket formation—a fact demonstrated at operation.

In the great majority of the cases repeated aspiration after thorough cocainization of the skin was performed without any great discomfort. The absence of any drainage tube through the chest wall permitted the patients great freedom of movement, both while in bed and later when they were walking about.

It is difficult to discuss the amount of time necessary for treatment by this method because of the limited number of cases treated. All of the patients were kept under observation in the hospital for a much longer period than necessary. This has lengthened considerably the average duration of stay in the hospital for this series of cases. Many of these patients were up and about the hospital for four or five weeks before discharge, receiving during this time one to two treatments a week. Such patients could be discharged earlier and have the occasional aspirations carried out in the out-patient department.

It is a very great pleasure to acknowledge the assistance of Dr. Frank J. Sladen and Dr. F. Janney Smith in the preparation of this report, and the aid received from Drs. L. G. Byington, L. S. Fuller and R. L. Schaefer, whose careful observation and treatment of the patients contributed largely to the success of the treatment.

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THE ADVANTAGE OF SERUM THERAPY AS SHOWN BY A COMPARISON OF VARIOUS METHODS OF TREATMENT OF ANTHRAX.

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Various methods of local therapy of anthrax have been in use for many years past, and are still widely employed either alone or in conjunction with other measures. If one has the time to consult the literature dealing with the subject, whether it be in periodicals or in text-books, it is at once evident what wide differences of opinion exist as to the most effective method of treatment. This is unfortunate and is liable to lead one to the conclusion that most all the usual methods give about the same results and it is not therefore a vital matter which one is employed in the individual case. This view-

point must be changed, as there is now accessible certain indisputable facts which prove it to be incorrect. Almost all the measures of local therapy in common use possess too many disadvantages to be considered locally effective, and they are uniformally without claim to a specific effect once an anthrax septicemia has originated. Some of them have even the danger of increasing the possibility of this latter grave complication (septicemia) supervening.

An ideal method of therapy for anthrax is one which fulfils best the following points: (1) It should be appliable to the various forms and locations of the disease; (2) should have the lowest mortality rate; (3) should be as specific as possible; (4) possess no danger of generalizing the local infection; (5) offer the least amount of scarring and deformity; (6) cause a minimum of pain; (7) entail the shortest absence from employment.

To draw any conclusion as to the method which best fulfils these points, the various measures of therapy in use must be first reviewed and their advantages and disadvantages considered.

Thermocautery is one of the oldest methods of treatment known (Schwartz[1]), and despite its many objectionable features it is still widely employed in many parts of the world. It is an extremely painful procedure, and when the lesion is extensive, especially when on the face or neck, it leads to hideous deformity, and prolonged convalescence if the patient recovers. It destroys rather indiscriminately both dead and living tissue, and unless applied thoroughly, which is surely an heroic measure in voluminous anthrax, it may seal off from free drainage tissue which is still infective.

Moreover, the barrier zone to the infection which nature has established may be in part or entirely broken down and generalization may thus originate. The treatment is not in the least specific, and when an anthrax septicemia exists is of no avail. For all these reasons it should be entirely omitted from the therapy of the disease.

Chemical caustics have been widely used in anthrax. Many writers advocate them as the only method of treatment, but in the majority of instances they are advocated as secondary measures. Among the caustics recommended are chloride of lime, nitric acid, zinc chloride, carbolic acid, bichloride of mercury and caustic potash. Graef[2] has reported a mortality of 5 per cent in 38 cases, and Scharnowski,[3] Bidder,[4] Arnozan Laude and Maranger[5] report successful results. The latter three authors, however, have abandoned the procedure owing to the vivid pain which ensues. That the method is uncertain the experience of Morosof[6] shows, for he has been unsuccessful in 2 cases, although in 1 he gave twenty-eight injections of 3 per cent carbolic acid and in the other seventy-six injections of 4 per cent carbolic acid in the depth of the pustule. Amory and Rappaport[7] report 3 recoveries by combined excision and cautery, but in 1 instance it required twenty days for the bacilli to disappear on culture from the lesion, and in another the patient

recovered only after three months. Whitla[8] mentions 2 per cent iodine for local injection and Chauffaud and Boidin[9] report the use of subcutaneous injections of 1 per cent carbolic acid and a solution of Gram's iodine. They admit that the latter solution is horribly painful and both are equally inefficacious.

Chemical cauterization has many of the same contra-indications mentioned under thermocautery. The possibility of poisonous effects or nephritis originating is an additional danger. Superficially applied these caustics are only palliative, and to be in the least effective the application must be thorough, and with many it should be repeated. Their lack of specificity is evidenced also by the diversity of the chemical solutions recommended.

Surgical intervention in the therapy of anthrax comprises two forms—incision and excision.

Incision has fallen in much disrepute as a mode of treatment, especially in Italy and France. Yet it is still often used, both here and abroad, particularly in instances in which the physician fails to recognize the disease and believes he is treating an ordinary carbuncle. The danger of the method was long ago recognized by the French physicians. Guerin,[10] Faucon,[11] Richard,[12] Chambert[13] and more recently Despres[14] warn of the danger of an erysipeloid or purulent inflammation of the wound setting in following operation. It is characteristic that patients treated by incision commonly develop the more severe types of the disease, and not infrequently die. Verneuil[15] gives interesting statistics on this point: "Among 6 patients so treated all died."

Incision has no place in the therapy of anthrax. It is not only contra-indicated but is actually dangerous. The operation breaks down the barrier zone to the infection and opens wide the blood and lymphatic channels of absorption, at the same time failing to remove the infected focus. As a result, increase in the extent of the local involvement and grave possibility of a generalized infection supervening are to be expected. It is also to be remembered that Marchoux[16] showed experimentally in animals that anthrax bacilli multiply rapidly in blood-clots, as they are not then so susceptible to leukocytic activity. Instead of assisting in the cure the operation further endangers the patient's life.

Excision at the present time is the most commonly used method in the therapy of the disease. It is, however, so frequently combined with thermo or chemical cautery or with serum that it is difficult to tell to which the results obtained are mostly attributable. Courtellement and Weill-Halle,[17] Dudley,[18] Ellitrop[19] and Raymond[20] are among the advocates of the method. Dudley combines the treatment with cauterization and serum, as used at Guy's Hospital, London, while Ellitrop administers anthrax vaccine. Some surgeons, among them Paget and Gosselin[21] and Despres,[22] believe that one should never resort to excision no matter what the location of the

lesion. Picaud[23] and Pratorius,[24] the latter on the basis of his extensive experience with anthrax, advise against excision. Müller[25] and Hiss and Zinsser[26] have found it impossible to prevent the spread of the disease in guinea-pigs by immediate excision of the site of inoculation. Scholl[27] recently compared the results obtained by the surgical and non-surgical treatment in 51 cases: 4 (44 per cent) of 9 cases treated surgically died while only 3 (7 per cent) of 42 cases treated non-surgically succumbed. One patient only recovered after amputation at the shoulder-joint. In conclusion, he states "that in several of the surgical cases a rapid increase in edema, a steady decline in the patient's general condition and death several hours later definitely pointed to the operation as a causative factor."

Excision despite its advantages over incision and thermo or chemical cautery has certain outstanding limitations and disadvantages. Thus in anthrax of the face it will always be objectionable from the esthetic viewpoint. Likewise when the neck is involved, if the disease is at all extensive, excision leaves often an extensive surface devoid of skin, with resulting scar-tissue formation and contracture, and, if skin-grafting is not performed, convalescence is much prolonged. The pain of the operation and possible hemorrhage must also be considered. Probably the most frequent source of danger is the difficulty of accurately defining the area to be excised, especially when the edema and induration are marked, as microscopic sections have at times shown bacilli far beyond the exact limits of the pustule in the edematous zone. To excise less than the entire area involved is to subject the patient to the pain and discomfort of the operation without a compensatory result in the way of a certain cure. On the contrary, as Nature's barrier zone is broken down and the blood and lymphatic channels are opened, the danger, local and general, of disseminating the infection is much increased. Since anthrax in man is primarily a local disease and usually remains thus—any treatment which may tend in the slightest way to generalize the infection is scarcely to be looked on as proper therapy. Once a septicemia exists the treatment is only palliative. Then, again, bacilli may persist in the wound for almost three weeks after operation (Rappaport and Amory's case), and in the presence of blood-clots rapid multiplication may occur. For all these reasons the writer believes excision should likewise be omitted from the routine therapy of the disease.

Various other methods have been advised locally in anthrax, many of which are only palliative measures, and some of which are claimed to be somewhat specific. Among the former may be mentioned wet dressings of various antiseptics, as advocated by Verneuil[29] and pulverization with bichloride, as advised by Savini,[30] All these measures evidently exert their action too superficially to be of any direct curative value and are at best only secondary measures. They may provoke inflammation, as Ricaud and

Launoy[28] have pointed out. The value of the subcutaneous injection of oxygen locally into and around the pustule, as recommended by Thiriar[31] and Theiry,[32] has not been established; moreover, anthrax bacilli grow well in atmospheric oxygen. Ramstedt[33] in 7 cases and Müller[34] in 13 have employed symptomatic treatment and rest with complete success. Such measures, while useful adjuncts to a more specific method, cannot be relied on alone, and it represents an attitude of therapeutic nihilism to allow a disease to take its own course if a remedy of proved value is at hand. The use of steam as advocated by Gucciardello[35] is too severe a measure for routine employment and its specific nature is not proved.

In the second group may be mentioned powdered ipecac, arsphenamine, extract of Bacillus pyocyaneus and normal beef serum.

Muskett[36] reports the successful treatment of 50 cases with ipecac paste locally. Both he and Washbourne[37] have experimentally found ipecac to destroy readily anthrax bacilli. This treatment, while not to be relied on alone, owing to what impresses one as a too superficial action, is a useful supplementary measure to a more specific mode of therapy.

Fortineau[38] uses extract of Bacillus pyocyaneus on the basis of antagonism existing between that bacillus and anthrax. He reports 32 cases, with 1 death. Further reports are necessary to establish the value of this local method. It has not been proved to be effective in anthrax septicemia, and the question of its value in the more virulent types of the local disease is still to be settled. It is not usually accessible for use, which is another disadvantage.

Arsphenamine has experimentally been proved of value by Shuster and Laubenheimer,[39] Laubenheimer[40] and Becker.[41] Each reports a recovery in septicemic cases with the drug. The results are encouraging but the treatment is in its experimental stage.

Normal beef serum has been advocated by Kraus, Penna and Cuenca.[42] They report a total of 415 cases with 4.3 per cent deaths. In the last 180 cases treated there were 11.6 per cent deaths, or 3.4 per cent, omitting intestinal cases. Lignieres[43] denies the value of beef serum in anthrax and reports experiments to prove his contentions. Kolmer[44] has also recently shown that while beef serum contains some antibactericidal properties it is without demonstrable protective and curative value in experimental infections in mice and rabbits.

Hutyra[45] has proved that immune anthrax horse serum gives higher protection in test animals than normal serum. In a recent article[46] in current literature the value of beef serum is again repudiated. Therefore Kraus's contention must still be accepted with reserve until such a time as normal beef serum has been shown to be experimentally and practically as effective as anthrax serum. In the absence of immune serum, normal serum may be tried until the former is obtained.

Anti-anthrax Serum. The credit for the original production of this serum is due to Marchoux, of France, and Sclavo, of Italy, both investigators publishing their work in 1895. Marchoux succeeded in immunizing sheep to anthrax by use of attenuated cultures, according to the method devised by Pasteur, Chamberland and Roux, and then by hyperimmunization with virulent cultures, in increasing doses at intervals of a week, obtained a serum possessed of both prophylactic and therapeutic properties.

Marchoux[16] showed that an immune sheep serum of (1–200 titer) was curative for rabbits in doses of 7 c.c. when it was inoculated at the same time or seven hours after the subcutaneous inoculation of $\frac{1}{3}$ c.c. of virulent anthrax culture. It was likewise effective in preserving life in 10 c.c. doses when it was injected twenty-four hours after the virus.

Sclavo,[47] working along somewhat similar lines to Marchoux, using, however, larger animals, at first goats and later asses, succeeded in producing a potent serum for use in human cases of the disease. As recently prepared, 10 c.c. of the serum thus obtained protects a rabbit from 0.5 c.c. of fresh virulent broth culture. Sclavo immunizes his animals over a long period of time, often as long as two years. Sobenheim[48] has modified the original methods of immunization further by employing simultaneous inoculations of anti-anthrax serum and culture, the latter being at first attenuated and later highly virulent, and given in increasing amounts until the animals (sheep) could withstand enormous doses. The serum was injected on one side of the animal's body and the virus on the opposite side. The serum obtained thus had the usual prophylactic properties for experimental animals (rabbits) in 10 c.c. doses, and also protected non-immune sheep (2 out of 5 animals) inoculated with a virulent anthrax culture in doses of 40 c.c. given from ten minutes to six hours after the cultures. Sobenheim used his method of immunization with complete success in a herd of 2700 cattle without any deaths or ill-effects attributable to the inoculations and with the complete disappearance of any further cases of anthrax among them.

Sclavo serum has been used extensively in Italy and South America both prophylactically and therapeutically in cattle and also in the treatment of the disease in man. It has, however, been very little employed in this country, and it is only in the last few years that the serum treatment of anthrax has come at all into use in the United States. The more frequent employment of immune serum in human cases of the disease is in no little part due to the fact that for the last few years the Bureau of Animal Industry in Washington has been preparing and has been distributing on request a very potent anthrax serum.

The credit for the perfection of this very potent serum is due to Dr. A. Eichhorn,[49] formerly chief of the bureau, and his collaborators.

In an attempt to find a more satisfactory method of immunization than those now in use they resorted to combined immunization with potent anthrax serum and carefully standardized spore vaccine, and found this method to possess marked advantages over the older Pasteur method. (The Pasteur method possessed certain hazards either in that the vaccine was too weak to protect or too virulent to be safely used[50]). During the progress of the work repeated occasions arose to treat a considerable number of afflicted animals with the serum thus produced, and remarkable recoveries were obtained in a very high percentage of the cases, including some of the more severe types. Comparative tests were made of this serum and several of the European makes and the American product was revealed to be twice as potent. The serum has been shown to have great therapeutic value in malignant pustule in man. Later by an improved technic, modelled along that which Banzoff used for diphtheria antitoxin, success was attained in fractioning and separating off the globulin content which contains the concentrated antibodies. This globulin serum has also proved its potency both in numerous tests on laboratory animals and practically in larger animals—cattle and horses.

The Bureau of Animal Industry has been furnishing state and city hospitals with the serum upon request for several years past, but in a recent communication from the bureau the writer learns that it is not their intention to continue this practice, inasmuch as several of the biological firms are now prepared to furnish such a product.[50]

Statistical Study of Anti-anthrax Serum. Picaud[23] believes that anti-anthrax serum has an incontestable efficacy, and to prove this refers to statistics of Pagliani.[51] In Italy from 1890 to 1900 there were recorded 24,052 cases of anthrax with 5812 deaths, or 24.16 per cent. On the contrary, statistics of these late years during which serum was used show 160 cases with 10 deaths, or 6.25 per cent, and in these 10 cases Pagliani states that the serum was employed too late to expect anything of the treatment. In 130 cases observed in Argentine Republic and treated by Sclavo[23] serum the mortality is considered by the writers as reduced to zero, the few cases that happened to die being attributable to secondary infection. In 1903 Sclavo[52] reported 164 cases treated by serum with only 6.09 per cent of fatalities. Legge[53] collected 12 cases of anthrax treated by serum in England between 1904–1905. Of these, 4 were treated by serum alone, 3 recovered and 1 died; while of 8 treated by serum plus excision, 6 recovered and 2 died. Of the fatal cases the serum was not administered until the day of death in one case and in the other case not until twenty-four hours before death, the dose being only 20 c.c. in the latter.

Herley[54] has reported 8 cases of anthrax treated by Sclavo serum with 1 death, excision being performed also in all but 1 instance.

Royer and Holmes[55] have reported 15 cases of anthrax, 4 of which were treated without serum with 1 death, and 7 by Sclavo serum plus surgical intervention with 1 death. These 11 cases comprised the more serious in which the lesion was located on the face or neck, while in the remaining the extremities were involved 3 out of 4 times. Schwartz[1] has collected a series of 68 cases occurring in New York state. His statistics show 17 cases treated by serum and rest with 5 deaths and 12 recoveries, and 28 cases treated by serum and excision, in one of which excision was close, with 26 recoveries and 2 deaths. Page's[56] statistics from English cases of anthrax threated with serum show an apparently higher mortality than in untreated cases. In the earlier group of cases the apparently high mortality was due to use of too small doses (10 to 20 or 30 c.c.), and in the later group the serum was often administered *in extremis*.

Pied,[57] in 1913, states that up to that date he found reports of 7 cases of anthrax with generalized blood infection which had recovered following serotherapy and 2 in which serum was used without success. Bandi,[58] in 1904, reported 2 remarkable cases of recovery in patients with an anthrax septicemia following energetic serum therapy. The first patient had been ill four days with a lesion on the forearm treated by thermocautery, and although the latter was thoroughly applied the process rapidly advanced, and when Bandi was called the man was comatous, with a temperature of 104° and a cloud of albumin and casts in the urine; 150 c.c. of serum was given immediately intravenously and 50 c.c. more the same evening. One and a half days later the temperature was normal, the patient conscious, the blood culture negative, the urine cleared up and the edema confined to the pustular zone. The second case was very similar and equally remarkable. Becker,[59] Bissell[60] and Graham and Detweiler[61] have each reported a case of malignant pustule with septicemia which recovered following the use of anti-anthrax serum. In the case of Graham and Detweiler excision was performed on the fourth day of the disease but failed to control the malady. In fact, within twenty-four hours afterward the blood culture became positive. On the sixth day 80 c.c. of anthrax serum and 100 c.c. of chloramin-T (Dakin) were given intravenously and complete recovery ensued.

Sclavo, Buron and Jager and Becker[62] have also demonstrated that anthrax serum is an efficient means of cure of even an anthrax septicemia in which the mortality by any other method is 100 per cent. All agree that under the influence of serum intravenously the bacteria rapidly vanish from the blood stream.

Rappaport and Amory[7] have reported a severe facial case with marked edema recovering rapidly after 80 c.c. of serum intravenously. Armour[63] cites an interesting case in which serum was not used until the seventh day of the disease, when the patient was in danger of suffocation. Within four days the patient was convalescent. A total of 60 c.c. of serum was given.

Mendez[64] has reported 1073 cases of anthrax with a death rate of 4.19 per cent treated by means of a serum he prepared himself by a method similar to that of Sclavo, the fatalities being due in the few fatal cases to the use of serum in moribund patients, to edema of the glottis, to myocarditis, to atheromata or to alcoholism.

Legge[53] in his very thorough article has examined the details of all published cases he could find up to January, 1905, treated by serum, namely, 67 in number. Of these, 56 were treated by serum alone and 11 by serum and some other treatment with a total death rate of 9 cases. In 44 of the 56 cases in which details would allow conclusions, marked improvement had taken place not only in the general symptoms but in the arrest in the further development of the pustule and in diminution of the edema by the third day. The average duration of treatment in these 44 cases was eight days. In none was it more than fourteen days. No visible scar or only a slight scar was present in all cases except 2, in which there was some loss of tissue, despite the fact that the face and the neck were involved in 35 of the 44. In 7 of the 9 fatal cases the patients were in a serious condition with widespread edema when the serum was administered and in all death occurred within thirty hours, usually in twelve, after the serum was given. Moreover, the doses of serum used in fatal cases were small, usually 20 to 30 c.c., and only one dose was given, and that apparently subcutaneously. In only 2 cases was the dose repeated a second time.

Cicognani[65] reports some remarkable facts in connection with the serum treatment. In Santa Croce, in Italy, a town of 5000 inhabitants with 36 tanneries, where Cicognani has adopted the serum treatment exclusively, the workers now insist on having this treatment to the exclusion of every other, and since operative interference is unnecessary, present themselves when there appears the smallest pimple suggestive of anthrax. Cigognani remarks on the rapidity with which improvement in the general condition occurs, often within a few hours, and the pustules dry up within a few days, while convalescence is much shortened. Lockwood and Andrews[66] and Stretton[67] have each reported a successful case treated by serum. In each instance the lesion was on the face and excision was contraindicated from an esthetic standpoint. The writer[68] has previously reported 2 cases and has since treated 5 more successfully by Eichhorn serum. The recovery in all instances was extremely rapid; convalescence was established within a few days after serum treatment was begun. The pustule in all instances rapidly dried up in a minute and a almost invisible scar was the only remains of the disease. The specific influence of the serum was so marked as to leave no question in the minds of the observers of the value of the treatment. The lesion was not excised in any of the 6 cases. Ascoli,[69] of Milan, uses serum often as the only treatment in doses of 5 to

15 c.c., sometimes repeating the injections five or six times in the same day. Sclavo[70] has lately stated that doses of 10 to 50 c.c. of serum are too small and that 60 to 80 c.c. is a minimum. Many authorities advise 40 c.c. Pagliani[51] has drawn certain conclusions in regard to treatment by anthrax serum: (1) The serum even in large doses is absolutely innocuous; (2) it is well supported even if given intravenously; (3) it may save the patient when the prognosis is hopeless; (4) it arrests rapidly the local process and reduces to a minimum the destruction of tissue.

Modat[71] believes in the efficacy of the serum treatment of anthrax and uses doses as high as 60 c.c., repeating the injection in twenty-four hours in doses of 20 to 30 c.c. and continuing this until the disease is controlled. Modat states that veterinarians sometimes use as much as 500 c.c. to 600 c.c. of serum at one dose in anthrax infections in horses. He quotes the work of Cuica in Bucharest, who has prepared an immune serum and relies on it exclusively in therapy. This writer has reported 40 cases, in 6 of which serum was not used, with 100 per cent mortality, the remaining 34 all recovering under serum therapy.

Dr. Douglass Symmers,[83] director of the Laboratories at Bellevue Hospital, reported recently "that within the past few years some 15 cases of anthrax have been treated in that hospital with specific serum and the results have been very gratifying; that while as one readily understands, all of the cases which had become septicemic with anthrax bacilli when first seen died, those which came under the serum treatment early were speedily cured, good results being apparent within forty-eight hours and recovery taking place within a week or ten days." The method of treatment followed has been to give 40 c.c. of Eichhorn serum intravenously every four hours, and at same intervals to inject 10 c.c. into the skin surrounding the pustule. Excision which was formerly used as a routine with serum or alone has been abandoned.

The reported cases of anthrax in New York City in the last few years have been as follows:

Year.	Cases.	Deaths.
1915	13	9
1916	4	3
1917	16	9
1918	15	4
1919	14	9
1920	12	1

During the early years of this period, 1915, 1916, 1917, serum was little, if at all, used. During the following years it began to be more employed but was combined usually with other methods of treatment, mostly excision. Finally, during 1920 serum has been fairly uniformly used and excision has been given up by many hospitals.

Hubbard and Jacobson[85] summarize the treatment in the 34 cases that have occurred in New York City during 1919 and 1920. The table is as follows:

	No. cases.	Recoveries.	Deaths.
Anti-anthrax serum only	14	12	2
" " " and incision	5	4	1
" " " and excision	4	3	1
" " " and chemical cautery	2	0	2
Chemical cauterization and incision	2	1	1
Anti-anthrax serum, excision and chemical application	1	1	0
Chemical application	1	1	0
" " yeast	1	1	0
No treatment recorded	4	0	4

Hubbard and Jacobson comment upon therapy thus: "As 14 cases recovered without operation and 9 recovered with operation it would be logical, to judge from the observed cases, that it was best not to operate. Again, out of the 14 that received only anti-anthrax serum 2 died. Out of the 12 that received serum aided by other treatment 4 died. The method which seems most successful is that of administering anti-anthrax serum, 10 c.c. by local infiltration every eight hours and 40 c.c. intravenously every four hours."

Comment on Serum Therapy. From the review of the statistics just quoted I believe certain conclusions may be drawn. From the standpoint of mortality in very large series of cases, anthrax serum has evidently the lowest death-rate of any treatment. Still there are very low mortality rates reported in fairly large but isolated series of cases by other methods, such as those of Kraus and his collaborators with normal beef serum, of Graef with caustic potash, of Muskett with powdered ipecac, and of Fortineau with extract of Bacillus pyocyaneus. Mortality alone however is not the only factor to be considered in selecting the ideal method of therapy for anthrax; other points previously referred to must also be considered.

At first, offering as it did a new method of therapy, anthrax serum was used like diphtheria antitoxin in the more desperate cases, often very late in the course of the disease, and this fact accounts for many of the early non-successes. Relatively few failures have occurred with immune serum which cannot be traced to either of the following facts: (1) To its use too late in the course of the disease within twelve to twenty-four or thirty-six hours of death; (2) to the employment of too small doses (20 to 30 c.c.); (3) failure to repeat the injections frequently, say every six to twelve hours; (4) use in persons with chronic disease, such as alcoholism, syphilis, chronic nephritis, myocarditis, etc.

The number of recoveries in cases that are considered hopeless is a most important comparative test of any measure of therapy. In anthrax septicemia immune serum has given the highest number of successes. In internal anthrax it should always be used, as it is

the only instrument of treatment worthy of the name, and we have yet to see what may be accomplished with a potent serum used properly. It is to be recalled that Mitchell[72] has seen cases presenting all the symptoms of pulmonary anthrax recover under serum therapy.

Immune serum therapy fulfils best the points mentioned as requisite for an ideal method of therapy. It offers the least pain, a minimum of scarring and is appliable to all forms and locations of the disease. It entails a shorter absence from employment than any other method with the exception possibly of excision. The serum is specific and is the only safeguard we have against generalization of the infection.

In this country we are especially fortunate in having accessible for the past few years a serum possessed of strong therapeutic properties as that prepared by the Bureau of Animal Industry. On the basis of the experimentally proved prophylactic value of this anthrax serum, as well as its incontestable efficacy in the treatment of the disease in both man and animals, there is now no longer any excuse for failure to utilize it in the treatment of all forms of anthrax, but especially of malignant pustule, in which the mortality can probably be reduced to a negligible one by early diagnosis and prompt serum therapy.

The specific action of the serum upon the course of the disease will rarely be questioned by those who have had an opportunity to employ a reliably potent preparation. Examples have been cited above which illustrate this, and they might be multiplied if space allowed. The prompt subsidence of constitutional symptoms, sometimes within twenty-four hours, and the rapid improvement in the local lesion, often within a few days, are the rule and not the exception. Statistics adverse to serum therapy are impossible to find if Page's[56] reports be excluded.

An argument that has been advanced against the use of serum is the expense of the treatment. Thus $30 has been quoted as the cost of production of the amount of serum required for the initial dose. Eichhorn[73] states that at present the serum sells at the rate of 5 cents per c.c., so in this case the initial dose should not cost any more than from $5 to $10. At this rate the entire cost of the treatment for an average case would not exceed by much the figure previously given by some writers as cost of the initial dose.

General Administration of Serum. The esential aim in the administration of serum is threefold: (1) To bring about a subsidence of the local lesion; (2) to counteract whatever toxemia may exist; (3) most important of all, to anticipate and prevent the development of an anthrax septicemia, or to try to control the blood infection if it exists when treatment is begun.

An outline of a method of administering anthrax serum, including the dosage and interval between doses in the various types of the

disease, may be of practical use, as the writer has been unable to find any such plan in the literature reviewed. It is perfectly logical that a severe or septicemia case requires larger and more frequent doses than a mild case.

At the beginning of treatment a blood culture should always be taken. The result gives one an index of the severity of the case and of the extent to which serum must be pushed. During the interval elapsing before the result of the blood culture is known, usually twenty-four hours' treatment must be energetically pursued in all cases, even the mild and moderate ones, because occasionally constitutional symptoms may be misleading as to the existence of a septicemia. Whether in all cases in this interval of twenty-four hours it would be best to follow the method of Symmers,[83] to give 40 c.c. every four hours, remains for later studies to show. The writer believes, however, that at present the following may be submitted as a tentative plan:

In Absence of Anthrax Septicemia. 1. In mild cases of the disease with little constitutional disturbance and a small well-circumscribed lesion with little edema the serum need not be given more often than every eight to twelve hours and commonly not more than three or four injections of 50 c.c. each (Eichhorn[74] recommends 50 c.c.) intravenously in the first twenty-four hours are required. The subsequent injections may be given at twelve to twenty-four hours' interval, depending on the progress of the case, commonly not more than six injections being required, the last few intramuscular or subcutaneous. Local serum therapy, as described below, should be used every twelve to twenty-four hours.

2. In the moderate cases, with medium-sized lesion and a moderate degree of edema and induration associated with definite constitutional symptoms, the serum should be administered for the first twenty-four hours by intravenous injections in doses of 50 to 80 c.c. (Eichhorn[74] recommends 50 to 100 c.c.) every eight hours, the subsequent treatments and frequency being in accordance with the progress of the case, commonly not more than six to eight injections being required, the last two or three intramuscular or subcutaneously. Local serum therapy should be employed for the first few days every twelve hours.

3. In severe cases, with large, voluminous lesions and extensive edema with or without marked constitutional disturbance but with negative blood culture, the serum should be administered by an intravenous route, either in small doses frequently repeated, 40 c.c. every four hours, or in larger doses at less frequent intervals, 80 to 100 c.c. (Eichhorn[74] recommends 100 to 200 c.c.) every six to eight hours for three or four more injections until the disease is controlled, when the intramuscular or subcutaneous route may be used in part and the doses reduced to 50 c.c. at intervals of twelve to twenty-four hours. Local serum injections should be given every six to eight hours for the first few days.

In Septicemic Cases. In such instances with a lesion as just described we have to deal with a most fatal disease, and it seems to be the consensus of opinion that the use of serum must be in unusually large doses and frequently given, the treatment being energetically continued until after the blood culture is negative. In such cases the injections would appear to be indicated every three or four hours intravenously in doses of 100 to 150 c.c. (Eichhorn[74] recommends 200 to 300 c.c.), and this treatment is continued until the septicemia is checked or the patient succumbs. Salvarsan may yet prove a useful adjunct in these desperate cases. The injection of serum locally should also be given every four to six hours.

In internal anthrax it would seem that a similar method of therapy to that used in septicemic cases would be in order. Anthrax serum should likewise be used intraspinally in anthrax meningitis.

Local Serum Therapy. It is evident in the review in the first part of this article that while many writers advocate diverse methods of local therapy, *i. e.*, cauterization, incision, excision, injection of chemicals, application of steam vapor, etc., a considerable number have combined these measures with serum therapy, evidently not trausting to them alone to bring about a cure. Since the only danger of the disease, rare cases of suffocation excepted, is the dissemination of the infection into the blood stream, the question of the advisability and necessity of these measures comes up. The prime essential in successful treatment is evidently to guard against blood infection, and this may be accomplished by (1) the general (intravenous and intramuscular) and local administration of immune serum, and (2) by avoiding the use of any local measure of therapy which might tend to generalize the local disease.

The measures of local therapy in common use are so severe and have so many disadvantages, such as pain, scarring, disfigurement and danger of disseminating the infection, to which attention has been called in detail above, under their appropriate headings, that the writer[68] in treating his own cases hesitated to resort to any of them. The only measure recommended which seemed to have no disadvantages and be of some therapeutic value, but probably more palliative than curative, was the application of wet dressings of powdered ipecac. This was therefore tried. In order to obtain an additional and more active and probably effective measure of local therapy it was decided to try the effect of the injection of serum into the lesion itself.[68]

It was considered probable that the introduction of the serum into close contact with the pustule would not only possess great advantages over other local methods previously advised but would actually be an additional precaution against an anthrax septicemia thus originating and might well have a decidedly beneficial influence upon the evolution of the lesion. As previously reported,[68] the method consisted in the injection of 2, 2.5, or even 3 c.c. of serum

at each of three or four points equidistant from one another at the various sides of the pustule. The needle is best inserted into the red indurated border of the pustule just beyond the blanched zone, the serum being directed toward the base of the eschar and injected so as to circumscribe the lesion. The injections are given once, twice or three times in the twenty-four hours, depending on the severity of the case, and not more than 7 to 10 c.c. are injected at one time. Commonly four to six injections suffice. A 5 c.c. glass Leur syringe and a fine-gauge needle are used in giving the treatment. The method has proved practically successful as the most desirable measure of local therapy. The writer has reported 2 cases previously and has subsequently treated 5 cases, all terminating in recovery despite the fact that the pustule was located either on the face or neck in all instances.

Local use of serum theoretically seems logical. The serum is then supplied in a most concentrated form at the site of the infection. The importance of this fact has been previously expounded on by Flexner[75] in relation to various bacterial inflammations situated in locations in which they receive a diluted and modified lymph secretion, as in massive inflammations, abscess formations and infections of serous cavities. While anthrax is not mentioned by Flexner in this excellent treatise[75] on *Local Specific Therapy of Infections*, the similarity to a massive inflammation and abscess formation is obvious. As examples of previous local use of serum in infections certain facts may be cited. Speiss[76] has shown that incisions infected with virulent streptococci have been controlled in the rabbit more surely by the application of the corresponding antiserum locally to the wound than by injecting it intravenously. Romer[77] has shown that pneumococcus keratitis is benefited by the direct instillation of antipneumococcus serum into the eye. Likewise, Netter[78] has recently succeeded in preserving vision by the injection of antimeningitis serum into the vitreous chamber of the eye in a case of epidemic meningitis complicated by suppurative choroiditis, a complication always resulting in loss of vision.

The character of the local inflammation in anthrax is of a peculiar type.[79] The serous discharge from the pustule during the first several days of the disease and often until the end, especially in fatal cases, is characteristically poor in leukocytes. The pathological anatomy of the lesion, as shown by Cornil,[80] Wagner[81] and Straus,[82] shows a very definite tendency for segregation of the anthrax bacilli in the center of the pustule, in which they are intertwined in a compact network practically free of leukocytes, the latter being distributed most densely as diffuse infiltration at the margins of the lesion and in the subjacent cellular tissue. In the more malignant cases and in the early stage of the disease, phagocyte activity is not much in evidence. Since the serum has been shown to have a marked effect in facilitating phagocytosis (Mar-

choux[16]) it is evidently logical to supply it in a concentrated form at the site of the pustule. In this way the normal resistant processes are strengthened, phagocytosis is increased and the inflammation is more quickly terminated.

The writer is glad to say that Symmers,[83] of Bellevue, has recently adopted the local serum therapy of anthrax as described above and reports very satisfactory results. Graham,[84] whose experience with anthrax has been quite extensive, in a recent article also endorses local serum therapy, and comments on the success that has attended its use when combined with the intravenous administration of serum.

Summary. 1. The various measures of therapy in use in treatment of malignant pustule have been reviewed. Statistics have been quoted showing comparatively the mortality with different treatment.

2. The disadvantages of the various measures of local therapy in common use have been discussed and attention has been drawn to the dangers that many of them possess.

3. The history of the development of anti-anthrax serum has been outlined. All the available statistics and facts relative to serum therapy of the disease in the foreign and domestic literature have been quoted so that conclusions might be drawn as to the value of the method. With marked uniformity reports of those who have used immune serum are favorable to the method.

4. The advantages of serum treatment over the other methods have been outlined.

5. A plan of dosage and interval between doses in the various forms of the disease has been tentatively given.

6. Local serum therapy has been described as a method of local treatment to replace the older and more dangerous measures. Its practical application and theoretical basis have been discussed.

Conclusions. 1. The measures of local therapy of anthrax in common use should be abandoned, owing to the disadvantages or even dangers they possess. These disadvantages include scarring and disfigurement, pain, danger of secondary infection being introduced, liability of spreading the disease locally or into the circulation, prolongation of convalescence and, but most important of all; their lack of any specific effect upon the course of the malady and their uselessness when the pustule is voluminous and when a septicemia has originated. The pustule is best left to its own evolution rather than to employ the more radical measures, owing to their tendency to disseminate and generalize the local disease, while the palliative measures exert their effect entirely too superficially for any direct curative value.

2. The value, both prophylactic and curative, of anti-anthrax serum must now be regarded as established by statistics. Its wellnigh specific nature in the therapy of the disease must be recognized

by the profession. The mortality from malignant pustule will be reduced to a minimum by prompt recognition and early serum treatment.

3. No case of anthrax septicemia should be considered beyond hope until intensive serum therapy has failed.

4. The serum prepared by the Bureau of Animal Industry or according to their method has been proved of marked potency, being according to certain reports twice the strength of the European preparations.

5. As originally described by the writer, the local injection of anthrax serum into the pustule is apparently the most effective means of local therapy and should always be used as a supplementary measure to the general administration of serum.

6. Anthrax serum fulfils best the points requisite for an ideal method of treatment of anthrax: (1) It is appliable to all forms and locations of the disease; (2) yields on average the lowest mortality rate; (3) is a specific measure; (4) is a safeguard against generalization of the local disease if used in time; (5) offers the least amount of scarring and deformity; (6) causes a minimum of pain; (7) demands on an average the shortest absence from employment.

7

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RECURRENT ADENOMYOMA OF THE UTERUS.

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Adenomyomata of the uterus comprise an interesting and important group of uterine tumors not only from their immediate clinical and pathologic aspects, but also from the fact that they may be potential foci for such complications as ectopic pregnancy or subsequent malignancy. The work of Cullen, which indicated a source for adenomyomata from the mucosæ of the derivatives of the Müllerian ducts, and particularly the endometrium, has supplanted the earlier conception of von Recklinghausen and his followers, who claimed that the glandular elements in such tumors arise from the Wolffian ducts. Subsequently further investigations have confirmed the observation of Cullen, and, in addition, as a factor of significance, it has been shown that portions of mucous membrane very similar to and apparently allied with endometrium may occur in places other than their normal position. In his monograph on *Adenomyomata of the Uterus*, Cullen cites the finding of normal uterine mucosa upon the serosal surface of the cervix and suggests the probability of origin for the epithelial elements in these tumors from such aberrant patches. Prior to the efforts of von Recklinghausen, in 1896, adenomyomata of the uterus received scant investigation, and it is greatly due to the stimulus of those studies that after exhaustive research the later views of Cullen and his associates were established. True it is that many worthy observers yet hold with the earlier hypothesis of von Recklinghausen, while still others, as, for example, Ries, are conciliatory, granting that since the Müllerian and Wolffian ducts are so intimately associated embryologically the adenomatous portions of these tumors might arise from either organ. Nevertheless the definite procedures pursued by Cullen demonstrated with sufficient conclusiveness that the epithelial structures in adenomyomata of the uterus arise directly from the uterine mucosa.

The incidence of adenomyoma of the uterus varies within narrow limits. In a series of 3388 hysterectomies for myomatous growths of the uterus (1906–18) at the Mayo Clinic, McCarty reports 211, or 6.43 per cent, of adenomyomata, while in 1283 myomata of the womb Cullen has found 73, or 5.7 per cent, of adenomyomata, exclusive of cornual nodules. The statistics compiled at the Magee Pathological Institute of Mercy Hospital at Pittsburgh showed 47, or 4 per cent, of adenomyomata were present in 1200 uteri removed because of myomatous growths. The condition presents a clinical

picture so closely resembling that produced by other myomatous growths of the uterus that preoperative differential diagnosis is difficult. In the Mayo Clinic series no case was diagnosed as such prior to the pathological analysis of the specimen. The age incidence of adenomyomata uteri enjoys a wide range in that the tumor has been found in a patient nineteen years of age, and also in some sixty years of age, with, however, the most frequent occurrence between the ages of thirty and fifty years. The association of pregnancy and collateral pelvic pathology with the finding of adenomyoma apparently have no significant interpretation. Any attempt to classify or group adenomyomata of uterus clinically would be futile. Therefore the anatomical grouping described by Cullen is here accepted as the working basis: Group I. In which the uterus maintains a normal contour, *i. e.*, adenomyoma diffusum benignum. Group II. Subperitoneal or intraligamentary adenomyomata of uterus. Group III. Submucous adenomyomata of uterus.

In the literature numerous instances of the association of carcinoma and adenomyoma as separate tumors within the same uterus are quoted, but few allusions are made presenting a definite tendency toward malignant change within the gland structures of the adenomyoma. This feature is prominently introduced in the case at hand and its presence lends an enhancing interest in view of the triple recurrence of the pathological and clinical findings. Hartmann and Lecene report the occurrence of a benign diffuse adenomyoma of cervix which manifested all the local symptoms and signs of cervical malignancy. Littlewood and Stewart recount the paired findings of adenomyoma and adenocarcinoma in the same uterus but as distinctly separate neoplastic processes. Cullen also details the possibility of multiple pelvic lesions in company with adenomyoma, and quotes instances of definite malignant development within the epithelial structures of the tumor. Von Recklinghausen is concerned with only 2 occurrences of carcinomatous change within the adenomyomatous tissue in his extensive series, while Meyer narrates 1 of doubtful validity.

The following case was admitted to the service of the late Dr. X. O. Werder, to whom I am indebted for the clinical records:

Case History. The patient, a single woman, aged forty-three years, entered Mercy Hospital, December 4, 1917, complaining of irregular, profuse and painful menstruation, with a mildly irritating intermenstrual watery discharge. At times she would not menstruate for five to six months, but recently has been bleeding every three weeks. The menses were profuse, exhausting and lasted five to seven days, being accompanied by severe pains in the back and general weakness. Her general appearance and nutrition were good. There was no weight loss and the important functions, aside from the menses, were normal. The hemoglobin was 70 (Sahli) and the erythrocytes numbered 4,300,000. Bimanual pelvic examination

revealed a firm mass about the size of a small orange occupying the vagina and protruding by means of a narrow pedicle through the cervix from within the uterine cavity. The exposed surface of the tumor mass was necrotic. The uterus was symmetric and not enlarged. The tumor was removed by vaginal myomectomy. After removal the specimen consisted of several irregularly torn fragments of tumor tissue removed from the uterus. The larger fragments showed partial covering by intact endometrium but elsewhere there was superficial necrosis. Some of the smaller and thinner plaques appeared as though they might have been portions of a cyst wall. Throughout the larger masses, numerous small, oval, honeycombed areas of pin-head size were observed, some of which contained a pearly, mucoid material. Microscopical sections of the mass from the uterus showed a dense, waving and interlacing fibromuscular structure, through which were irregularly distributed abundant gland structures. These varied markedly in size and shape, some being small or oval, while others were dilated, cystic and of irregular contour. Although a few tortuous spaces were noted, presenting for the most part empty lumina, nevertheless some of the cavities contained a homogeneous, mucoid material. The lining epithelium was of a tall columnar type and uniform throughout. Where the glands were dilated the parenchymal cells were to a degree flattened. Nuclear figures were not observed and there was no evidence of invasive qualities or atypical growth. It was noteworthy that not a few of the acinar structures were surrounded by a richly cellular stroma of concentric arrangement, as is seen in normal endometrium. Occasional mitotic figures were observed in the nuclei of these stroma cells. Still other alveolar elements were inserted directly between the muscle fasciculi of the tissue and displayed no accompanying stroma. The pathological diagnosis was adenomyoma uteri.

Fourteen months later (February 1, 1919) the patient again sought the hospital, with a return of all the clinical symptoms which preceded the first operation, and, in addition, a definite metrorhagia with its resultant secondary anemia. Pelvic examination disclosed a large firm mass the size of a fetal head tightly wedged in the vaginal cavity. A vaginal myomectomy was repeated and by virtue of the firm impaction of the mass in the vagina it was necessary to remove it piecemeal. The tumor, as in the case of its predecessor, hung into the vagina from within the uterus by means of a slender fibromuscular pedicle.

Several variously sized pieces of tissue from the uterus, portions of which were discolored and superficially necrotic, were removed at the second operation. The surfaces of the tissue elsewhere were of a pale pink or red, moist, glassy appearance and in places showed a normal mucous membrane. On section through the fragments islands of pearly gray tissue were encountered which at intervals showed microscopic cyst cavities of varying size and containing a

gelatinous gray or brownish material. The tissue was edematous and could be easily crushed between the fingers. Microscopical sections of the tissue presented a dense, though edematous, fibromuscular structure, throughout which were scattered islands of glandular tissue. The alveolar structures varied greatly in size and shape, some being tortuous and at times contained a mucinous material. The acinar epithelium was of columnar type and occasionally surmounted a cone-like shaft of stroma which projected into the lumen in the manner seen in intracanalicular fibro-adenoma of the breast. However, at no place was there any reduplication of the lining epithelium, no nuclear figures were observed, and there was no violation of the basement membrane nor papillary formation by parenchyma. For the most part the glands lay in a concentrically arranged, moderately cellular stroma which now presented rather marked myxomatous change. The pathological diagnosis was adenomyoma of the uterus.

Three months following this operation (May 2, 1919) the uterus was found to be slightly enlarged. Eight months subsequent to the second operation (September 24, 1919) the patient returned, complaining of almost continuous bleeding. Pelvic examination showed the uterus to be considerably enlarged but quite regular in contour. Abdominal hysterectomy was advised and executed, there being removed an enlarged uterus, amputated above the cervix, and the attached adnexa of both sides. The uterus was opened through the posterior wall and measured 13 x 9 x 5.5 cm. When reconstructed, the serosal surface was smooth, regular and yielded no evidence of tumor within the organ. The myometrium was very thick, especially at the fundus where it varied from 2.7 to 3.3 cm. in thickness. Toward the cervix it measured 1.7 cm. The uterine wall was tough, with apparently an increased fibrous connective-tissue content, and the blood channels therein were tortuous and thick walled. On opening the uterus three distinct tumor masses were found. The largest one occupied almost the whole of the posterior wall of the organ and had been cut through; the second, a smaller one, about the size of an English walnut, nestled high in the fundus; while the third, which formed a symmetrical bulging of the uterine wall, presented itself upon the anterior surface. The uterine cavity was large and lined throughout by a thick intact endometrium of healthy appearance, which was carried in unbroken continuity over the projecting tumor masses. The large polypoid mass on the posterior wall projected well into the uterine cavity and for a distance at its juncture with the myometrium was sharply demarcated, but for the greater part merged almost imperceptibility with the muscular coat. On the cut surface this tumor measured 7.0 x 3.8 cm. Its surface presented a variously nodulated contour and was covered by an intact mucosa which dipped into the mass to meet the irregularities of conformation. Section through the tumor mass

revealed a variegated appearance. At places the tissue was quite firm, gray, smooth, glassy and not easily crushed, while other areas displayed numerous thin-walled cysts containing a clear straw-colored fluid. The latter structures varied markedly in size and radiated in a cluster-like manner from a central fibrous core, to which they were attached by a slender pedicle. These grouped cystic clusters gave this portion of the tumor an appearance not unlike that of hydatidiform mole. The small cysts could be easily ruptured and the linings were smooth. This peculiar cystic formation gave the mucosal aspect of the tumor its peculiar appearance. At places the endometrium dipped into and over irregular cavitations in the tumor, the walls of which were composed of a thick, pale

Opened uterus, showing three tumor masses.

membrane. On opening such membranous sacs their inner lining in turn was observed to be studded by inward projecting, lobulated, cauliflower masses. No more than a thin watery fluid was found in such cavities. At one point on the surface an oval, sessile bulging was noted which contained two small typical cauliflower masses. These hung from a narrow base into the otherwise smooth, empty cyst. At the juncture of the tumor mass with the myometrium several rather large channel structures were observed, and these, too, presented the characteristic fungoid papillary projections into the otherwise smooth-lined cavities. It is noteworthy that these papillary ingrowths were somewhat more easily crushed than the remainder of the neoplastic tissue. The smaller nodule in the fundus was about the size and shape of an English walnut. Its mucosal

covering was complete and the component tissue was of soft consistency. This mass also presented the characteristic cysts with a pale membrane comprising the cyst wall and the typical polypoid cauliflower projections into the cyst cavities, as noted in the larger mass. Several cysts in this instance were filled with a chocolate-colored fluid. The nodule was not sharply defined against the underlying uterine musculature, although it did not invade the myometrium to any great depth. The oval sessile symmetrical elevation on the anterior wall was quite firm and was covered by an intact endometrium. On section through the compact uterine wall a pearly, opalescent area, implanted directly into the surrounding opaque myometrium, was encountered about 3 mm. beneath the mucosal surface. No definite cysts could be determined in this area, and it was indistinctly differentiated from its environs.

Microscopic analysis of the tumor tissue of the uterine wall showed a compact fibromuscular structure in large whorls. Gland structures of varied size and shape were quite regularly and abundantly scattered through the tissue. Some of the cysts were elongated or stellate. In the greater number the lumina were empty, but occasionally there was contained in them a homogeneous material. Not infrequently the irregular stellate acini presented definite bulgings into the lumina, due to the projection of a slender shaft of stroma tissue. These papillæ were almost invariably surmounted by a single layer of columnar epithelium and imparted a picture not dissimilar to that presented by an intracanalicular fibro-adenoma of the breast. In the majority of instances the lining of the glands was of a tall, columnar-cell type, fairly uniformly arranged and occasionally showing definite cilia. The cell nuclei were, as a rule, quite large and vesicular. Nevertheless in some instances, and particularly where the glands were most tortuous, the lining epithelium manifested a definite tendency toward proliferation or showed a papillary ingrowth into the lumen. At rare intervals mitotic figures were observed in the nuclei of the epithelial cells. In no instance did the mucosal cells violate their basement membrane or exhibit high invasive qualities. It is of interest to note that many gland structures were surrounded for varying widths by a more or less concentrically arranged stroma very like that seen about the normal endometrium, while the remaining glands, devoid of supporting stroma, were inserted directly between the muscle fasciculi. Nuclear figures were seen quite frequently in this stroma tissue. The sections displayed no evidence of an inflammatory reaction. The "flowing in" of the endometrium deep into the interstices between the muscular whorls was well demonstrated in the sections.

The triple recurrence of a supposed benign growth is of sufficient import to merit painstaking investigation, and to the clinician is the occasion of no slight misgiving. The clinical diagnosis of the condi-

tion prior to the first and second operations were sarcoma uteri. It is interesting to note that at the present time, three years after the beginning of the condition and fifteen months subsequent to the hysterectomy, the patient enjoys improving health and manifests no evidence of metastatic involvement. The materials furnished by the earlier operations consisting only of projecting tumor tissue afforded an opportunity for no more than a purely speculative study as to the true intra-uterine status. As above stated the recurrence of a neoplastic process signifies grave possibilities to the surgeon, and so, too, to the pathologist when attempts at complete surgical removal have been made. However, in this instance the failure to extirpate the foci of growth would probably explain the repetition of the pathological state. Nevertheless over and above this are presented certain gross and microscopic characteristics of unmistakable significance. With the two earlier specimens a very definite picture of adenomyoma was portrayed. The tissue masses were evidently of the usual fibromyomatous character covered in places by a healthy mucous membrane and containing numerous gland structures of innocent nature. The third specimen presented an enlarged but symmetrical uterus which, when opened, revealed three distinct tumor masses. The large area on the posterior wall and the smaller one high in the fundus were quite similar in structure. In general they were seen to be made up of a peculiar combination of cysts and fibromuscular tissue. The latter, however, was somewhat more easily crushed than in the normal myometrium. The cysts were formed of a thin membrane lined by smooth endometrium and usually containing a clear or brownish-tinged fluid. From the walls of several of these cysts, projecting clusters of cauliflower appearance jutted into the cavity. These projecting clusters could be easily crushed between the fingers and were strangely suggestive of tissue met with in carcinoma uteri. Throughout the irregularities of conformation in the tumor the endometrium persisted in unbroken fashion. Microscopical analysis corroborated previous diagnoses of adenomyomata of the uterus, but here and there the reduplication of the lining epithelium of the glands or papillary projection into the gland lumen were strongly suggestive of early malignant neoplasia even though no definite invasive characters were as yet manifest. In addition the extreme irregularity of the glandular acini and the occasional finding of nuclear figures in the alveolar epithelium gave added weight to the view. The difficulty in making a diagnosis of early carcinoma requires no more comment than to allude to the extreme caution with which one approaches the interpretation of differential stages in papilloma simplex, recurrent papilloma and carcinoma of the larynx. The dividing lines in the process of neoplasia are most delicate and rest more or less upon accessory factors gleaned in ways other than from the microscope alone. Certainly, on this occasion, the microscopical analysis of

several of the gland structures, in addition to very suggestive appearances in portions of the gross specimen, lend weight to the possibilities of very early malignant change despite the fact that such is contra-indicated by both the mass of the general pathological findings and the clinical progress of the patient.

By virtue of the fact that adenomyomata were so intimately grouped with other myomatous growths of uterus it was not until the searching efforts of von Recklinghausen, in 1896, that these tumors received special attention. The champions of this author's views that the glandular elements in such tumors arose from the Wolffian duct were numerous. It is quite possible that the work of this group stimulated Cullen to a more exhaustive study of these growths with the resultant production of his monograph on *Adenomyomata of the Uterus*. Subsequent publications recording the discovery of myomatous tumors with glandular inclusions in various portions of the pelvis and lower abdomen give greater prominence to the far-reaching conclusions of Cullen. Firmly of the opinion that the gland structures in adenomyomata arose from Müllerian duct mucosa, particularly endometrium, the latter observer demonstrated clearly the direct continuity of such structures in the endometrium with those in the tumor mass. The peculiar "flowing in" of the uterine mucosa between the fasciculi of myometrium in the third specimen herein described coincides with the opinion expressed. Other features supporting this view are the characteristic stroma of normal endometrium accompanying many of these glands and the fact that the parenchymal cells possess cilia. Beyond clearly defining the origin of adenomyoma, Cullen is also concerned with the distribution of these tumors in the body, their clinical manifestations, complications, prognosis and treatment. Ries in his article concerning "Nodular Forms of Tubal Disease,"[7] assumes the middle road, not attempting the differentiation of one embryonal development from the other, and suggesting that because of the intimate association of the Müllerian and Wolffian ducts during their development it is reasonable to accept the theory that either organ may participate in the formation of adenomyomata.

In discussing adenomyomata of the recto-vaginal septum, Cullen remarks that the histopathology in such tumors is exactly identical with that seen in similar growths occurring in the uterus and that the glands appear as uterine endometrium out of place. The discovery by Cullen that normal uterine mucosa may at times be found upon the serosal surface of cervix could well be explanatory of the development of these tumors in such extra-uterine sites quite independent of the possibilities of migration from the uterus directly. Sir John Bland-Sutton details the finding of an adenomyoma of the uterus involving the rectum. This tumor presented the characteristic microscopic picture of an adenomyoma and probably represented an original growth in the uterus which subsequently

became subserous by extension and thereafter involved the rectum. Further studies of adenomyomata of the recto-vaginal septum were reported by Curtis and Jessup, both of whom portrayed typical features of such growths in their descriptions.

In 1916 Cullen described a tumor occurring in the round ligament in which were numerous cysts. Of the latter some contained a clear fluid while others were filled with a chocolate-colored material. The tissue, the writer asserted, was suggestive of adenomyoma. Almost simultaneously there appeared in another journal an article written by the same author, dealing with an adenomyoma of the round ligament and incarcerated omentum in an inguinal hernia, in which he felt assured that the tumor was a true adenomyoma. One of the earlier reported cases of adenomyoma uteri was that reviewed by Hellier, in 1913, wherein he noted the absence of sharp demarcation of outline about the tumor, so characteristic of this neoplasm, and observed the typical gland arrangement so similar to that of endometrium with the accompanying stroma of uterine mucosa in abundance. Gough and Stewart cited the triple location of adenomyoma in a patient who presented the tumor in the uterus, Fallopian tube and sigmoid colon. In each instance the macroscopical and microscopical findings were analogous and the mucous structures in the neoplasms were very much similar to those of normal endometrium. The reason for the implantation of the growth in so distant a locus as the sigmoid colon is open to conjecture, although, as before noted, the finding of tumor containing uterine mucosa far removed from the uterus is now not uncommon. The occurrence is apparently somewhat akin to the findings of the observations of Leitch, who investigated an adenomyoma beginning in the posterior wall of the uterus, which migrated or was extruded through the serosal surface and attached itself to the sigmoid colon. Later the glandular elements in the tumor infiltrated the wall of the colon. Among other observers who have described typical adenomyomatous growths in places far removed from the endometrium was Schwarz, who, in the course of relating the details of an adenomyoma of the recto-vaginal septum, noted that these tumors, or at least tissue like endometrium, did occur in the ovaries. Concerning this feature there is little information given. However when the relationship of the sex gland and the Müllerian duct structures during the embryological development of the female is understood the discovery of uterine mucosa in the ovary may lose its perplexing attitude. In this regard it is interesting to note that Casler described a peculiar diffuse uterine tumor in which the stroma of endometrium was abundant, but at no place were parenchymal structures observed. At a subsequent laparotomy upon the same patient the left ovary was removed and on pathological analysis presented a stroma-gland arrangement analogous to that of normal uterine mucosa.

The greater portion of the evidence gleaned from the work of

recent investigators lends support to the opinion of Cullen as to the derivation of the glandular elements in adenomyoma uteri. Were more details of information required to firmly establish such views they are furnished through the reports of two rather curious cases. Bell performed a hysterectomy on the second day of the normal menstrual period. Pathological examination of a large tumor mass contained within the uterus demonstrated a characteristic adenomyoma save that the glands were dilated and filled with a dark blood clot indicating that the alveolar structures were participating in the menstrual phenomenon. The utilization of a specificity allotted only to derivatives of the Müllerian system is strongly suggestive of the direct origin of the glandular structures quite aside from the repeated proof furnished by histological study. So, too, Doederlein and Herzog recount the occurrence of a true pregnancy within one of two loculi in an adenomyoma of the uterus. Truly the continuity of the mucous surface lodging the fertilized ovum with that of the endometrium cannot be doubted, for otherwise there is no explanation for the ectopic implantation of the germinal cells. Fortunately the observers were able to demonstrate the communication between the endometrium and the dilated gland cavity containing the placenta. The wide range of distribution of adenomyomas containing uterine mucosa has been recently published by Cullen. The writer indicated that tumors composed of unstriped uterine muscle and containing uterine mucosa were to be found in the uterus, the recto-vaginal septum, tubes, round ligaments, utero-ovarian ligaments, utero-sacral ligaments, sigmoid flexure, rectus muscle, umbilicus, and that quantities of uterine mucosa may occasionally be found in the ovaries.

Little further comment need be made upon the association of carcinoma of uterus with adenomyoma. There is no indication that there might be any direct relationship between the two conditions even though the incidence is more than occasional. Cullen denoted the moderate frequency of such paired findings while MacCarty estimated 5.5 per cent of the uteri removed for myomatous growths at the Mayo Clinic presented concurrent, independent malignancy of the cervix or body. Littlewood and Stewart reported the finding of the paired condition in a uterus, each occurring separately. Hartmann and Lecene related an interesting observation wherein a patient presenting all the local manifestations and physical findings of a cancer of the cervix was found on later pathological analysis of the surgically removed specimen to have been suffering from a benign diffuse adenoma of the cervix. Nor should there be any particular surprise that malignant neoplasia may occur in the acinar structures of adenomyomata. On the other hand it is rather remarkable that this pathological change has not been noted more frequently than has been reported at this time, for the tissues involved possess proliferative tendencies.

Concerning the clinical symptoms produced by adenomyomata, little may here be said other than that they are in general quite comparable to those produced by other myomatous growths of uterus. Cullen maintains that careful observation will yield features which will render possible a true differential diagnosis. On the other hand, MacCarty reports that not one of the 211 adenomyomatous uteri in the immense series of hysterectomies for myomatous growths of uterus was diagnosed as such before operation.

The writer wishes to express his appreciation to Professor Oskar Klotz for suggesting the study, and for his generous advice and helpful criticism.

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REVIEWS

INFECTIONS OF THE HAND. By Allan B. KANAVEL, M.D., Assistant Professor of Surgery, Northwestern Medical School, etc. Fourth edition. Pp. 500; 185 illustrations. Philadelphia and New York: Lea & Febiger, 1921.

THE reader should need no introduction to this book, the first edition of which came out some years ago. This, the fourth edition, is a result of a thorough revision with additions. The text has been supplemented with the knowledge obtained from the war upon gas bacillus and streptococcic infections as well as permitting the addition of a chapter upon the restoration of function in infected hands.

Experimental and anatomical studies are made, upon which the deductions are founded. Much emphasis and space is given to the pathological anatomy, for it is only by understanding and appreciating the underlying pathogenesis that a surgeon can correctly treat the hand infections.

The book covers the subject completely, thoroughly describing by text and illustration every condition and complication. A chapter on diagnosis and treatment in general shows into what group a particular case will fall and directs the student to the proper place in the book for the detailed treatment.

No surgeon should be without this excellent work and every hospital should have one available for reference, both for the surgeon and the intern. E. E.

MOUTH HYGIENE. A TEXT-BOOK FOR DENTAL HYGIENISTS. Compiled and edited by ALFRED C. FONES, D.D.S., Professor of Preventive Dentistry in Columbia University. Second edition. Pp. 334; 218 illustrations and 8 plates. Philadelphia and New York: Lea & Febiger, 1921.

THE dental hygienist is the most recent professional addition to the ranks of those ministering to the health of the community. Special training schools have been established in several universities and many states have enacted laws to govern the practice of dental hygiene. The young women who take up this work are

destined to play an important part in the prevention of disease. The establishment of this work on a professional basis is largely due to the pioneer efforts of Dr. Fones, whose ideas have been largely adopted as a foundation for the courses of instruction that are being given. In his book, aided by several eminent collaborators, he has set forth the dental and allied subjects that are essential for the education of the dental hygienist. The principal matters covered are: anatomy of the head, functions of the teeth, malocclusion of the teeth, inflammation, pyorrhea alveolaris, dental caries, dental disease in relation to general health, principles and technic of dental prophylaxis, and the broad field of service of the dental hygienist, especially in relation to hospitals, industrial clinics and public schools. R. H. I.

ROENTGEN INTERPRETATION. By GEORGE W. HOLMES, M.D., Roentgenologist to the Massachusetts General Hospital and Instructor in Roentgenology Harvard Medical School, and HOWARD E. RUGGLES, M.D., Roentgenologist to the University of California Hospital and Clinical Professor of Roentgenology, University of California Medical School. Second edition, thoroughly revised, pp. 228; 184 illustrations. Philadelphia and New York: Lea & Febiger, 1921.

IN the second edition of this splendid little volume the authors have made a number of corrections of defects that appeared in the first and, in addition to this the text has been thoroughly revised and new material and illustrations added. The simple expedient of placing arrows on the illustrations to indicate the lesions under discussion has greatly enhanced the value of the book. Very often a lesion that is quite apparent on a negative becomes just as obscure on a reproduction and in studying an illustration the reader has no little difficulty in locating just what the illustration portends to show. This is particularly true of line fractures and early bone and pulmonary disease. The indicating arrows relieve the reader of this difficulty and as a result the book is studied with much more satisfaction.

No pretension is made to present a finished treatise on any one subject. The purpose of the authors is to present the essentials of roentgen interpretation; this they have done concisely and well. For more detailed and specific information the reader is referred to the list of the most recent literature that is found at the end of each chapter.

Among the important new material in this edition is a brief description of some of the rarer forms of bone pathology, namely, Madura foot, parasitic cysts, yaws, Koehler's disease and chloroma.

J. D. Z.

EVOLUTION OF DISEASE. By PROFESSOR J. DANYSZ, Chef de Service, Institut Pasteur, Paris; translated by Francis M. Rackemann, M.D., Assistant in Medicine in the Harvard Medical School. Pp. 194; 1 illustration. Philadelphia and New York: Lea & Febiger, 1921.

IN Part I of this engaging little book "the various stages in the development of acute infectious diseases" have been traced and in Part II a theory of immunity, anaphylaxis and anti-anaphylaxis propounded, which if correct should have an extremely valuable application in the comprehension and therefore intelligent treatment of many chronic non-contagious diseases. Far be it from the present reviewer to pass judgment on the merits of a theory arising from such a source and involving problems of such scope and importance; but he can at least recommend to readers the perusal of a concise, interesting and suggestive treatment of the subject.

E. B. K.

MEDICAL ELECTRICITY, ROENTGEN RAYS AND RADIUM, WITH A PRACTICAL CHAPTER ON PHOTOTHERAPY. By SINCLAIR TOUSEY, M.D., Consulting Surgeon to St. Bartholomew's Clinic, New York City. Third edition. Pp. 1337; 861 illustrations, 16 in colors. Philadelphia and London: W. B. Saunders Company, 1921.

IN the first part of this book the author discusses the different kinds of electrical currents that are used in treatment, their modes of production, physiological and pathological effects, and the methods of applying them in diagnosis and therapy. In this part electrophysics is dealt with very thoroughly and at great length. No fault can be found with the quality of the text dealing with the physics of electricity, but there is entirely too much of it. It is easily appreciated why it is necessary for the specialist in this field to be familiar with the principles of electrophysics; it is quite as readily understood that this speciality can be intelligently practised without knowing, for example, how to measure the potential of a condenser or determine the horsepower wasted in the form of heat by the passage of a current of electricity through a wire. We do not argue that it is not an advantage to possess this purely technical knowledge, but it must be borne in mind that the primary interest of the physician lies in the diagnosis and treatment of disease and not in the construction of electrical machinery.

The chapter on electrodiagnosis is well done, as is also the one on electrical accidents and their prevention. The same thing, however, cannot be said about that part of the text that is concerned with the application of electricity in disease. There are doubtless many things in it that are of value despite the fact that in not a few instances rather extravagant statements are made in

extolling the virtues of this therapeutic agent. A claim of apparent cures in cases of angina pectoris by rubbing a vacuum electrode over the entire chest and applying electric vibratory massage to the abdomen, falls hardly within the bounds of conservatism.

In revising the text on Roentgen Rays, the author has failed to bring it up to date. As a whole this part of the book lacks balance. For instance, fifty-four pages are devoted to radiography of the teeth and about three-fourths of a page to the *x*-ray diagnosis of gastric ulcer and carcinoma, while the discussion on the duodenum is exhausted by two short paragraphs in which appears the remarkable statement that "radiographs, as a rule, do not show this part of the intestine at all, or only as a shadowy outline making a curve around the pylorus, with its concavity toward the left."

The last chapter is devoted to a discussion of radium, its physical properties and physiological effects. This chapter contains much useful information. J. D. Z.

A Laboratory Course in Serum Study. By Hans Zinsser, M.D., J. G. Hopkins, M.D., Reuben Ottenberg, M.D. Second edition, revised. Pp. 184. New York: The Macmillan Company, 1921.

This course outline of immunology for medical students has received but few important alterations since the first edition of five years ago. Most of these changes are in the form of alterations in the plan of experiments. E. B. K.

Operative Surgery. By John J. McGrath, M.D., F.A.C.S., Professor of Surgery, Fordham University, etc. Sixth edition. Pp. 863; 369 illustrations. Philadelphia: F. A. Davis Company, 1921.

This work is preëminently for the student and practitioner, and for the man learning his surgery. The text is arranged well and the subject-matter presented in a very readable manner, based on an anatomical or regional plan. Before describing the procedures the author gives a very complete practical outline of the anatomy of the part; preserved in a style and manner that robs it of its dry detail nature. Many of his anatomical points are further impressed upon the reader by illustrations.

The operative procedures are thoroughly and clearly outlined and illustrated, and should be clearly understood and readily followed by the operator.

The size of the book precludes any possibility of its being an extensive reference book on operative surgery. It does not attempt to describe every operation, but it does furnish the student reader a most complete and ready operative surgery for daily use. E. L. E.

VITAMINES—ESSENTIAL FOOD FACTORS. By BENJAMIN HARROW, Ph.D., Associate in Physiological Chemistry, College of Physicians and Surgeons, Columbia University. Pp. 213; 8 charts. New York: E. P. Dutton & Company, 1921.

A WORK couched "in terms of our everyday tongue" and designed to give the layman a working knowledge of nutrition. In chapters I–VIII the author builds for the reader a knowledge of the physiological chemistry of food. Chapters IX–XIV deal solely with vitamines and to the physician seeking fundamental knowledge of vitamines these chapters are recommended. For those who wish to delve into the subject more deeply, the appendix offers food tables and an extensive bibliography. The physician who has occasion to supply information to his patients, on foods or on vitamines, will do well to recommend Dr. Harrow's book, for the author has not taken any knowledge of the reader for granted. The only adverse criticism to be offered is that the title is too limited, as less than one-half of the book is devoted to vitamines.

E. T. C.

A TEXT-BOOK OF PATHOLOGY. By ALFRED STENGEL, M. D., Sc.D., Professor of Medicine, University of Pennsylvania, and HERBERT FOX, M.D., Director of the Pepper Laboratory of Clinical Medicine, University of Pennsylvania. Seventh edition, reset. Octavo of 1111 pp., with 509 text illustrations, many in colors, and 15 colored plates. Philadelphia and London: W. B. Saunders Company, 1921.

THE seventh edition of this text-book appearing after an interval of six years may be taken as sufficient evidence of its continued popularity. During the twenty-three years that have elapsed since the appearance of the first edition the number of pages has increased from 851 to 1111 and the text figures from 372 to 509. It is to be regretted, however, that neither author is actively engaged in the study of this subject as his major interest, and this may account in part for the fact that many of the illustrations of the first edition are still to be found in the just appearing edition, and that those borrowed from other sources constitute more than half of the total number of illustrations. As "replacements and additions of illustrations to the extent of about a hundred have been provided," this condition will perhaps be still further improved in the next edition.

The terminology of the section on bacteriology contains several peculiarities; for instance, the streptococcus intracellularis meningitidis would hardly be recognized by many younger students of bacteriology. Bacillus typhus is surely a more common designation of this organsim than bacillus typhi abdominalis. The authors

showed a pecular preference for bacterium and mycobacterium, over the customary term of bacillus. One regrets the omission of *B.* edematiens in the section on anaërobes and of Rickettsia prowaczeski in the designation of typhus."

One notices with pleasure the inclusion of concise paragraphs on Lethargic Encephalitis, Trench Fever, Influenza, Noguchi's Leptospira Icteroids and similar "novelties." The sections on nephritis and tumors of lymphatic tissue, rewritten for this edition and of particular interest to the senior and junior authors respectively, are for both these reasons of particular value. E. B. K.

SYPHILIS AND VENEREAL DISEASES. By C. F. MARSHALL, M.D., F.R.C.S., and E. G. FFRENCH, M.D., F.R.C.S., Lt.-Col. R.A.M.C. (retired). Fourth edition. Pp. 422; 96 illustrations (6 in color). New York: William Wood & Company, 1921.

IT is as great a pleasure to welcome the fourth edition of this book, whose premier volume appeared fifteen years ago, as it is interesting to see how far superior it is to the flood of similar literature, the apparent outgrowth of the War's stimulating experiences. This volume owes its worth, not alone by right of prior domain, but because of its clear presentation, its sane attitude, and its concise style. This edition has been greatly strengthened by having E. G. Ffrench as co-editor, adding materially in both experience and authoritativeness.

There is but one criticism, and that pertinent to all such efforts, *i. e.*, the impossibility of incorporating in so small a volume the entire field of venereal diseases; and yet we can frankly say that this is by far and away the most concise, readible, instructive and trustworthy treatise on these conditions that it has been our privilege to review. It is a splendid type of book to put in the student's hands, feeling confident that he will not be advised in error when following its teachings. A. R.

THE WASSERMANN TEST. By CHARLES F. CRAIG, Lieut.-Col., M. C., U. S. Army, Professor of Bacteriology, Parasitology and Preventive Medicine, and Director of Laboratories, Army Medical School, Washington, D. C. Second edition. Pp. 279; 3 colored and 10 half-tone plates. St. Louis: C. V. Mosby Co., 1921.

THIS book has been enlarged, carefully reëdited and brought up to date. The author touches upon the history of the Wassermann reaction; considers its specificity; discusses its underlying principles; gives detailed methods of its application, both for the

blood-serum and the spinal-fluid tests; and elaborates in a mature manner upon its interpretation under various conditions, involving duration of syphilitic infection and thoroughness of treatment. The author's modification of the test and that of the U. S. Public Health Service are given. The importance of considering isohemolysins within the different blood groups (Moss's classification), where the anti-human hemolytic system is employed, is emphasized. Colloidal gold, protein tests and cell counts on spinal fluids, with methods, are mentioned in conjunction with the Wassermann test, as they have bearing on the diagnosis of syphilis. The book throughout bears the authoritative stamp of the writer's rich experience. Especially valuable is the conservative interpretation of the Wassermann reaction in the light of available data in the different stages of syphilis and following treatment—an interpretation unbiassed by any pretext of placing personal skill in diagnosis, or the efficiency of any particular system of treatment in the foreground. The book is a safe guide for the laboratory worker, and yet admirably meets the needs of the clinician who wishes to be able to interpret the laboratory findings in syphilis, and to correlate them with his clinical observations. J. C. S.

TYPHUS FEVER, WITH PARTICULAR REFERENCE TO THE SERBIAN EPIDEMIC. By RICHARD P. STRONG, Professor of Tropical Medicine, Harvard University Medical School; GEORGE C. SHATTUCK, Medical Secretary, League of Red Cross Societies; A. W. SELLARDS, Assistant Professor of Tropical Medicine, Harvard University Medical School; HANS ZINSSER, Professor of Bacteriology, Columbia University; J. GARDNER HOPKINS, Bacteriologist of the American Red Cross Sanitary Commission to Serbia. Pp. 273; 26 full-page illustrations. Cambridge, Mass.: Harvard University Press, 1920.

THE campaign against the appalling typhus epidemic in Serbia, 1915—"one of the most severe which the world had known in modern times"—is described by Dr. Strong in an interesting and vivid manner. Perhaps, due to its occurrence before this country was thoroughly alive to the situation in Europe, this epidemic did not receive in this country the attention that its importance warranted. It is, therefore, correspondingly surprising to read that during the six months of 1915 in which the epidemic was at its height, typhus admissions to the military hospitals alone often reached 2500 per day. With a mortality varying between 30 and 70 per cent there was a total of over 150,000 deaths in Serbia alone, and to meet this terrible situation there were just 350 Serbian doctors available, with totally inadequate material supplies. The story of America's part in the organization of the International

Sanitary Commission and in the prosecution of the campaign which quickly brought the epidemic to a successful termination must be entered as one item to our credit in that difficult period before our tardy entrance into the war. The loss from typhus of 126 of the 350 Serbians and of 5 volunteer American doctors points to another chapter in the glorious history of the medical profession's combat with disease.

The history of previous epidemics and the etiology of typhus are discussed in detail. The mass of evidence points toward Rickettsia as the most probable cause, and its transmission by lice is regarded as of the greatest practical importance, though not yet definitely excluding droplet and other forms of infection.

The valuable clinical observations by Shattuck, based on 42 carefully studied case reports, with autopsy notes in 20 laboratory examinations by Sellards and bacteriological reports by Zinsser and Hopkins, add to the thoroughness of the presentation. Numerous illustrations and the pleasant format of the Harvard University Press complete the value of this contribution to epidemiological literature.

E. B. K.

GRAPHIC METHODS IN HEART DISEASE. By JOHN HAY, M.D., F. R. C. P., Honorary Physician, Liverpool Royal Infirmary; Honorary Consulting Physician, Ministry of Pensions. Second edition. Pp. 178. London: Joint Committee of Henry Frowde, Hodder and Stoughton, 1921.

THE first edition of this book was published in 1909. Since that time the use of graphic methods in studying heart disease has so far extended knowledge of the subject that it became necessary for the author to rewrite rather than revise most of the book. This has been done and the subject-matter brought abreast of present-day knowledge and beliefs.

The most of the book is devoted to the technic of the use of the polygraph and the interpretation of tracings. A chapter on the electrocardiograph has been added.

The material presented is well chosen, the tracings are excellent and the legends accompanying them fully explanatory. There are a few faults, mostly of minor type. For the sake of completeness, some attention should have been devoted to the rare abnormal rhythms such as auriculo-ventricular rhythm, ventricular escape and sino-auricular heart block. The classification adopted, which groups sinus arrhythmia and paroxysmal tachycardia together as disturbances of stimulus production, but classes extrasystoles as disturbances of excitability seems of rather doubtful utility.

The book may be heartily recommended to anyone desirous of beginning the use of the polygraph, likewise to those who wish to acquire proficiency in the reading of polygraphic tracings.

C. C. W.

PROGRESS
OF
MEDICAL SCIENCE

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY AND ASSOCIATE IN SURGERY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL AND NORTHEASTERN HOSPITALS AND ASSISTANT SURGEON TO THE UNIVERSITY HOSPITAL.

Trasplantation of the Ureters into the Large Intestine in the Absence of a Functionating Urinary Bladder.—COFFEY (*Surg., Gynec. and Obst.*, 1921, xxxii, 383) says that it was found in experimental work that the bile duct when implanted directly into a dog's small intestine always dilates, while a bile duct which has been transplanted and made to run immediately under the mucosa for a distance does not dilate. A ureter implanted directly into a dog's intestine always dilates and sooner or later the kidney is destroyed by pressure and infection. A ureter which has been transplanted and made to run immediately under the mucosa does not dilate as a rule. The author explains the dilatation universally found in direct implantation. The small intestine as well as the large is practically always found in a state of rotundity and partial distention, which he calls static intra-intestinal pressure. His second proposition was—how has Nature prevented this intra-abdominal pressure from reaching the inside of the normal duct? Dissection of the duodenum showed that the common duct passed through the wall of the intestine down to the mucosa and ran for a distance under the loose mucosa before emptying into the bowel. With a fountain syringe attached to a rubber bag and with a thin flap of rubber cemented over the inside of the tube's entrance, these same principles were demonstrated in a purely mechanical way. The modifications in technic and clinical application were devoloped by Charles H. Mayo.

Acute Intestinal Obstruction.—FINNEY (*Surg., Gynec. and Obst.*, 1921, xxxii, 402) says that early diagnosis is the most important factor. The shortness of the interval of time elapsing between the onset of the symptoms and the operation plays a most striking part. In 21 cases with operation within twelve hours from the beginning of symptoms, there were 20 recoveries and 1 death. The effect of the time element

can be still more strikingly seen in the steady increase of mortality with lengthened interval since the mortality of his entire series was 36 per cent. The author is impressed with the difficulty of definite diagnosis, for intestinal obstruction in many cases may be simulated by typhoid fever, Henoch's purpura, certain infections, appendicitis, acute pancreatitis, the twisted pedicle of a tumor, lead colic, renal colic, gallstones, mesenteric thrombosis, and diaphragmatic pleurisy. It is comforting to note, however, that most of these conditions demand operation almost as imperatively as bowel obstruction. Post-operative intestinal obstruction is often masked by the symptoms usually present in the first few days after operation. In cases of doubt it is safer to operate. The determining factors are the intestinal character of the vomitus, the failure of lavage and enemata to relieve the vomiting and an increasing pulse-rate with restlessness and thirst. The passage of the stomach tube in doubtful cases of this type may prove to be a means of avoiding reoperation if used with due intelligence. It is safe to say that approximately one-half of the cases of intestinal obstruction occurring in hospital and private practice have their origin in adhesions resulting from previous operative procedures. There has been no satisfactory explanation for some of the phenomena observed. It is probable that the two most potent factors are the presence of a persistent low grade inflammatory process, and the presence of some foreign body, such as unprotected gauze drains. Prevention of sepsis, careful handling of tissue and discontinuance of packing and repacking have helped much. Moreover, not much aid can be hoped for from artificial sources, such as the application to the peritoneal surfaces of ointments or membranes and the like. Paralytic adynamic ileus in some degree is probably of more common occurrence than is usually believed to be the case. Differential diagnosis between paralytic and mechanical obstruction is not always easy. These cases do not always look sick—abdominal pain is not marked, pulse rate is not much increased. Regurgitant vomiting is early pronounced but does not persist. After several days, in favorable cases, vomiting reappears—a sign of reëstablished gastro-intestinal activity. The pathology of this condition is still in doubt. The character of the anesthetic however, does not seem to play an important part, while infection is generally believed to be the most constant etiological factor but in the author's series the picture in a well developed case is rather that of a true paralysis of the sympathetic nervous system.

High Tracheotomy and Other Errors—The Chief Causes of Chronic Laryngeal Stenosis.—Jackson (*Surg., Gynec. and Obst.*, 1921, xxxii, 392) says that the most frequent cause of chronic laryngeal stenosis is high tracheotomy. The classic distinction between a high and low tracheotomy with reference to the isthmus of the thyroid gland is a relic of the days when too much respect was held for this structure. This distinction should be abandoned. There should be taught only one tracheotomy and that should be low. The trachea should always be incised lower than the first ring, except in those rare cases in which laryngoptosis renders this impossible without entering the anterior mediastinum. The cricoid cartilage should never be cut, unless laryngoptosis places all the rings of the trachea below the upper

border of the manubrium. If, in an emergency, a high incision of the trachea has been made a cannula should not be worn in it. As soon as the patient's breathing has been resumed a low incision should be made and the cannula inserted therein.

Suprapubic Drainage of the Bladder.—MOTHERSILL AND MORSON (*Brit. Med. Jour.*, 1921, p. 418) state that acute retention of urine has been relieved by puncturing the bladder with trochar and cannula for a considerable period. More recently, a process has been refined to facilitate drainage and prevent any leakage into the prevesical space or upon the external abdominal wall. In certain suitable cases the insertion of the self-retaining tube invented by M. DePezzer fulfils its purpose of draining the bladder from above the pubes without leakage or discomfort. This method of drainage can only be adopted when a good distention is to be obtained and no previous operation has been performed. When hematuria is present, the operation is contra-indicated because the DePezzer tube is readily blocked by clots. So simple a procedure reduces shock, a most favorable factor in subjects requiring suprapubic drainage prior to prostatectomy because of deficient excretion of urea. The subsequent prostatectomy is without the difficulty caused by the scarring of the abdominal wall.

Treatment of Syphilis.—MACCORMAC AND KERMAWAY (*Brit. Med. Jour.*, 1921, p. 415) says that the syphilis is but one process whether it involves skin, mucous membrane, nerve or other tissue. The principles upon which treatment is based vary in accordance with the duration of infection. When infection is recent, primary or secondary, two objects are in view: cure of the disease and prevention of communication to others. A severe and lengthy course of treatment should be undertaken. The authors by extensive tabulation have shown that six injections of salvarsan, (Novarsenobenzol used) 0.9 gm. per dose are often insufficient. The "10 injections" series proved satisfactory. At conclusion of these salvarsan courses, mercury was administered intramuscularly for three months. The condition of the Wassermann reaction was determined. If positive, the course was repeated from the beginning. If negative Wassermann was obtained, mercury either in pills or by injections is continued until two years have been completed. The Wassermann reaction was investigated every three months. The authors admit that such a course is severe and long but justifiable when balanced with the serious results of failure and delaying of cure, for as time passes the disease becomes fixed. In late stages of disease active forms of medication such as salvarsan and mercury, by inunction and injection are preferable to other methods. Ten intravenous injections of salvarsan were given followed by three months of intramuscular mercury. Repetition of this course is generally necessary.

Renal Decapsulation for Chronic Nephritis.—KIDD (*Brit. Med. Jour.*, 1920, p. 378) reports several cases of far advanced chronic nephritis, where this procedure has given favorable results. The technic of the operation is described. He believes that the lymphatics are unblocked by decapsulation and that another route is set up for drainage of lymph from the kidney for the lymphatics of the kidney run up from the ureter under the capsule through the kidney where they receive

the lymph of the kidney substance and then to the glands in the vascular pedicle of the kidney. Possibly in these cases of chronic nephritis the lymphatics become blocked either by excess of lymph or by fibrinous deposit and the nephritic poison cannot be drained away from the kidney substance. The author has noted that clear lymph seems to flow from the kidney sponge almost immediately after decapsulation.

Chronic Duodenal Obstruction.—KELLOGG AND KELLOGG (*Ann. Surg.* 1921, lxxiii, 578) say that chronic duodenal obstruction occurs more commonly than is realized and can often be diagnosed from the history and physical signs. The obstruction may involve the first or second portions of the duodenum only, due to ulcer, or gastroptosis or adhesions, or the entire duodenum, most frequently caused by compression between the vertebral column behind and the superior mesenteric artery in front, especially when there is traction in the direction of the pelvis from the drag of a distended and ptosed cecum and colon. The physical signs of obstruction in the first portion are those of pyloric obstruction. When the second and third portions are involved it can often be made out by percussion and succussion. The symptoms are those of epigastric discomfort and toxic manifestations. With a competent pylorus, cramp-like pains predominate. When incompetent, regurgitation of bile is frequent. Symptoms are often suggestive of ulcer, gall-bladder or appendicular trouble; in operating for these conditions with negative findings, the duodenum should be carefully examined. Medical treatment, consisting of abdominal support, nutritious diet and anti-constipation measures is beneficial in the majority of cases. Surgical treatment in obstruction of the first and second portions consists of freeing of adhesions, gastropexy or duodeno-duodenostomy. In the third portion, the procedure of choice is duodeno-jejunostomy. Duodeno-jejunostomy is indicated in vicious circle after gastro-enterostomy, accompanying gastro-enterostomy when the duodenum is obstructed, in obstruction of the third portion not responding to medical treatment. The author describes the technic and cites cases with a general summary of symptoms and results. Total number of reported cases is 58, with no mortality. In the author's series of 41 cases, only 1 was unimproved.

Enterostomy in the Treatment of Acute Intestinal Obstruction.—SUMMERS (*Surg., Gynec. and Obst.*, 1921, xxxii, 412) says in serious cases surgeons make a primary enterostomy as a life-saving measure or do a combined operation, making an enterostomy in the distended coils after successfully removing the cause of obstruction. The field has been still further broadened by including peritonitis ileus in the indications for operation. Formerly, Nealton's injunction to open the first coil of distended intestine for enterostomy procedure had been regularly followed. In 1910 Bonney advised opening the jejunum for this purpose, for it is the segment of toxicity when the vomitus becomes feculent. The positive proof of the value of this procedure in the circumstances is that drainage of the jejunum causes immediate cessation of vomiting. MacKinnon, in 1917, recommended strongly the simple modern drainage of the intestine by introducing a large-sized catheter and fastening it into position by a double purse-string suture. The catheter comes away in a few days with quick subsequent closure

of the abdominal wall. The author advocates jejunostomy when the vomitus is frankly feculent.

Injury to the Bile Ducts and Methods of Repair.—SWEETSER (*Ann. Surg.*, 1921, lxxiii, 629) says that interference with the normal flow of bile is due to a stenosis of the ducts following deep ulceration, pressure by adhesions and division of the common duct (intentional or accidental) during operation of cholecystectomy. The anatomical abnormalities and the presence of abnormal adhesions, congenital and acquired, must be carefully noted and guarded against in right upper abdominal surgery. The methods devised for restoring the bile stream to the intestine have been varied in order to meet the conditions encountered. In most cases the ends of the ducts are widely separated and the intervening space filled with dense scar-tissue. Simple approximation is no longer possible. Therefore, other means must be employed to bridge the hiatus. The tissues which lend themselves best to a successful and permanent anastomosis are those which normally are bathed in bile and consequently are immune to its irritation. When the mucous membrane of the bile duct, stomach or duodenum can be brought and held successfully to the proximal end of the duct, the result has been permanent in the majority of cases. Splinting with a soft rubber tube aids the process of repair. Failures have been due to stenosis or ascending cholangitis with abscesses in the liver. Attempts to bridge the gap with autogenous grafts have all failed in experimental animals. No human cases are recorded. An attempts was made by Murphy to utilize the biliary fistulous tract, but the patient died in eight months.

The Wassermann Reaction.—RAY (*Amer. Jour. Syphilis*, 1921, v, 320) says that in spite of the multitude of modifications and newer methods for the serodiagnosis of syphilis, the classical Wassermann reaction or a technic which departs from it only in minor details stands today as the only reliable laboratory test for syphilis. A series of 580 reactions, performed with crude and cholesterinized extract each with 2 methods of fixation namely, the one-hour incubator and the four-hour ice-box methods is analyzed with the following conclusions: A positive reaction with cholesterinized antigen alone should be given no specific significance in untreated cases presenting no clinical manifestatations of lues and giving a negative history. The four-hour ice-box method of fixation, while increasing the sensitivity of the cholesterine antigen as compared with the one-hour fixation in the water-bath magnifies the non-specificity except in treated cases, congenital syphilis and in some cases of neurosyphilis, where it has a decided advantage. On the other hand, with the crude extract, the four-hour ice-box method of fixation, while increasing the sensitivity does not impair but rather augments the specificity. The cholesterinized antigens possess a specific sensitivity exceeding that of crude in all cases of syphilis under treatment, congenital syphilis and in some cases of neurosyphilis. The great value and importance of lumbar puncture in all cases of syphilis is emphasized. A spinal fluid examination including cell count, globulin estimation, colloidal gold and Wassermann reaction is imperative before prognosis can be given in spite of the fact that treatment has produced a Wassermann negative of the blood.

THERAPEUTICS

UNDER THE CHARGE OF

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The Tonsillar Route of Infection in Pulmonary Tuberculosis.—ZWALUWENBURG and GRABFIELD (*Am. Rev. Tuberc.*, 1921, v, 57) have described a shadow which they believe represents a thickening of the pleura over the apex of the lung, and they have studied its relationship to tonsillar and cervical gland tuberculosis. They state that such apical pleuritis was seen in 10 per cent of the rœntgen-ray examinations made. Such apical pleuritis occurs most frequently in cases showing tuberculosis deposits in the faucial tonsils (93 per cent). With cervical gland tuberculosis this lesion is recognizable in 59 per cent of all cases and probably occurs in a larger number, being obscured by the shadows of pulmonary tuberculosis, 71 per cent in this group showing either this lesion or frank tuberculosis of the lung or both. Cases without tuberculosis of the tonsil show an apical pleuritis in only 11 per cent of the cases. It is suggested that a common route of infection may lie through the tonsil and cervical lymphatics to the apical pleura and thence into the lung. If this hypothesis is accepted it offers a singularly satisfactory explanation for the frequency of apical lesions, the predominance of right-sided lesions, of the pathogenesis of tuberculous pleurisy with effusion and other obscure features of this infection.

An Output Study of Users and Non-users of Tobacco in a Strenuous Physical Occupation.—BAUMBERGER, PERRY and MARTIN (*Jour. Indust. Hyg.*, 1921, iii, 1) present their second paper in a series of articles on the significance of the use of tobacco in industry, namely, the relation of the use of tobacco to efficiency in a strenuous physical occupation. They adopted output as the criterion of efficiency, and chose the bottle-making industry for their studies. They conclude that smoking has little effect on output rate in the strenuous physical occupation studied. Chewing markedly lowers output rate. Light smokers have a slightly lower output rate than heavy smokers.

A Survey of Carbon Monoxide Poisoning in American Steel Works, Metal Mines and Coal Mines.—FORBES (*Jour. Indust. Hyg.*, 1921, iii, 11) states that carbon monoxide, as met with in metal and coal mines and about blast furnaces in this country, rarely causes late after-effects following acute severe gassing. When such effects do appear, there is evidence, almost always, of a preëxisting pathological

condition. Frequent exposure to carbon monoxide causes headache and malaise, but no evidence has been found of a cumulative harmful effect. As was to be expected, owing to the compensating increase of hemoglobin and red cells from prolonged oxygen want, it is possible to acquire some tolerance to carbon monoxide. A recent advance in treatment has been made by adding carbon dioxide to the oxygen inhalations administered. Recovery is three times as rapid as when oxygen alone is used. An efficient portable carbon monoxide respirator has been perfected by the U. S. Government.

Superinfection in Experimental Syphilis Following the Administration of Subcurative Doses of Arsphenamine or Neoarsphenamine.—Brown and Pearce (*Jour. Exp. Med.*, 1921, xxxiii, 553) conclude that the existence of an infection with Spirocheta pallida does not constitute a bar in itself to the introduction and propagation of a second infection in the same animal; that, just as there is a period following a first inoculation during which a second infection may be implanted with the production of characteristic primary lesions, conditions may again arise in animals which have once become refractory to a second inoculation that will favor the introduction of a new infection with the formation of lesions presenting the characteristics of an original or first infection. Experimentally, such a state may be induced in rabbits with early but well-marked primary lesions of the testicles by treatment with either arsphenamine or neoarsphenamine; hence, treated but uncured animals may be rendered as susceptible to a second cutaneous inoculation as a normal animal, and the manifestations of disease resulting from the second infection may be indistinguishable from those of a first infection. The results obtained showed: (1) That the treatment employed was insufficient to cure any of the therapeutic controls; (2) that the infected controls were highly refractory to a second inoculation; (3) that the treated animals were highly susceptible to a second inoculation, and although not cured of their original infection, reacted to the second inoculation with the formation of lesions indistinguishable from those of a first infection; (4) that in certain instances the treatment given had rendered infected animals more susceptible to infection than the normal controls.

Treatment of Epilepsy.—E. Christin (*Schweiz. med. Wchnschr.*, February 3, 1921) writes that bromide medication is not wholly satisfactory in the treatment of epilepsy. The sodium salt should be employed to avoid the depressant action of potassium on the heart. Bromides may be given in smaller doses if the amount of chlorides in the diet is reduced as much as possible. The employment of the stimulating ammonium salt is considered irrational. Luminal is considered more favorably. It differs from veronal only in the substitution of a phenyl radical for an ethyl group, whereby it is asserted that the sedative effect is greatly increased. The daily dose consists of 2 grains, in cachets. For hypodermic administration, the soluble sodium derivative should be used. Luminal exerts its sedative action without unpleasant side-effects. A large number of observers recommend its use in rapidly recurring

epileptic attacks; it acts more quickly and surely than bromides but is less useful in petit mal. Potassium boricotartrate, in doses of 45 grains a day, has been successfully used by Pierre Marie. Here also the attacks are prevented without the depression frequently accompanying bromide therapy. The author concludes that luminal and perhaps potassium boricotartrate are the only new agents of value in the treatment of epilepsy. Christin speaks of the new conception of the nature of epilepsy developed by Hortenberg, who believes that inhibition has a large share in the development of the attacks. The main interest of this theory lies in the treatment evolved by Hortenberg. He employed strychnine up to as much as 2 grains by mouth; even these formidable doses never resulted in epileptic attacks but rather improved the condition of the patients.

Study of Oxytoxics.—GUGGISBERG (*Schweiz. med. Wchnschr.*, February 3, 1921) recommends pituitary extracts in the treatment of weak labor pains, but urges the necessity of initial small doses. Intravenous administration is the method of choice. Ergot is the mainstay after labor; if administered before the complete expulsion of fetus and placenta, tetanic contraction of the uterus may occur. Experiments on isolated organs showed that quinine in low concentrations caused more frequent contractions, and this effect lasted longer than that following pituitary extract or ergot. Large doses of quinine caused paralysis after an initial period of marked stimulation. Quinine never caused tetanus of the uterus. The dose of quinine during labor should be 4 grains of the sulphate, repeated after an hour. Quinine is also useful in the treatment of abortion, especially where non-operative treatment is indicated in the presence of active infection. Others have reported favorably on the addition of quinine to the narcotics used in the induction of twilight sleep. Quinine is recommended in the early stages of labor, pituitary extract during the second stage, and ergot at the end of labor. Guggisberg mentions investigations carried out with various combinations of drugs. The most favorable results were obtained from a combination of quinine and pituitary extract, and of ergot with placental extract. The author states that he has proved the existence in the placenta of substances stimulating uterine contractions, the action of which appears to render the uterus more sensitive to normal and therapeutic stimuli.

PEDIATRICS

UNDER THE CHARGE OF

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The Calcium Metabolism of Premature Infants.—HAMILTON (*Am. Jour. Dis. Children*, October, 1920) says that the calcium metabolism of premature infants has never been studied before this, but this study is justified by the fact that these infants are more liable to acquire

rickets than full-term babies. It is also a common experience that bone symptoms appear in the premature at an early age, and that the condition more often takes a grave course than in other infants. It has been assumed that this tendency is caused by the absence of a congenital store of calcium, supposed to be present in full-term babies. About 85 per cent of the body's calcium at birth is stored during the last two or three months of intra-uterine life, so that a premature birth exposes the body to postnatal life with a proportionately small amount of calcium. It is thought that this fact is partly responsible for the prevalence of rickets among the premature. The proportionately small amount of calcium in the body of the premature newborn may possibly lead to a state of calcium starvation in the course of postnatal growth. There are, however, in the postnatal growth of prematures often certain characteristic features which might also unfavorably influence the calcium metabolism. Although the difference in corporal development between the premature and the full-term newborn may be very great, there is in the healthy premature, when properly nourished and cared for, a great tendency to make good this difference. It is not unusual for such an infant to double its weight in three months, and triple it in six months. The question arises whether the tissues formed in the rapid recovery from an acute or chronic nutritional disturbance are of the same composition as in the more slowly growing bodies of normal infants. It is logical to believe that they are rich in water and poor in salts. The author made studies on 4 infants born from four to ten weeks before full-term. The causes of the premature births were advanced pulmonary tuberculosis in the mothers in 3 cases, and nephritis and eclampsia in the other 1. In the cases of tuberculosis the babies were separated from the mothers immediately after delivery. Symptoms of tuberculosis and syphilis were absent in all cases during the period of observation. The Wassermann tests were negative. The infants were nourished from birth exclusively on breast milk given in bottles. They gained rapidly in weight during the months in which the experiments were carried out. The stools at times were both frequent and loose both during the experiments and in the intervals. These were the normal loose and frequent stools that are frequently seen in babies on breast milk. Three of the 4 infants had a very low calcium retention during the first months of life. This might possibly be ascribed to rickets, as in all of the children craniotabes appeared in the second month. This is not in harmony with the fact that although the craniotabes increased in the months that followed, the retention of calcium increased to amounts found in normal infants. It was demonstrated that in those periods where the intakes exceeded 200 mg., the retentions are as large as in normal infants, while in the periods where the intakes were lower than this amount, there was sufficient retention in only 1 case. If sufficient retentions are to be attained, it would seem that the intake must exceed a minimum of 200 mg. The calcium is excreted mainly in the stool. The daily amount of feces excreted by prematures is very large, a fact that may be explained by the low fat absorption found in prematures. The daily values of the total solids are consequently higher than in normal infants, although the quantities of milk taken by prematures are very small. The calcium percentages

of the total solids were found to be lower than in normal infants, but not sufficiently lowered to counterbalance the excess in total solids and the small intakes. To balance these factors exceedingly low calcium percentages would have been necessary. An experiment where a normal infant was alternately fed with ordinary breast milk and breast milk fortified with fat demonstrated that a high fat intake may in the breast-fed infant lead to a temporary loss in calcium. The increased fat ingestion was followed by an increased fat excretion. During the experiment the feces took on the appearance of the feces in prematures. It was due to an excess in fat intake. In the prematures there is suggested an insufficiency of the digestive mechanism.

Butter Fat and the Child Weight.—Larson (*Arch. Ped.*, October, 1920) presents data from the weight charts of 10 children selected from a number in an orphan's cottage home. The weights were recorded at intervals of six months during two and a half years. The weights of 3 were incomplete for this period, due to the fact they were discharged before the end of this period, or had not been admitted at the beginning of the study. The cottages have a population of about 30 children, but because of the changes those who had not been for some length of time were not considered, and those who had received medical treatment were also not included. It was observed that there was a gain in weight for each six month period except the fourth. During this period the superintendent in compliance with the request of the Federal Government for food conservation, especially of the animal fats, had substituted oleomargerine for butter in the diet of the children. Nine of these 10 children lost weight during this oleomargerine period. The other child was a girl, who was considerably above the weight and height for her age, but her progress was retarded as compared with her gain during the previous and following periods. The 7 children whose records were complete for two and a half years showed a gain of their combined weights for the first three six month periods, but a loss of their combined weights for the fourth period, which was the time in which oleomargerine was used. There was again an increase of their combined weights for the last fifth-sixth month period, during which butter was again added to their dietary.

The Heart in Scarlet Fever.—Rosenbaum (*Arch. Int. Med.*, October, 1920) studied 1770 cases of scarlet fever. There were 106 patients with recognized cardiac complications, 94 of whom developed these complications during the course of the disease, and 12 were instances of old heart disease. Eighty-eight of these 106 patients or 5 per cent of all the cases had myocarditis. Of these 53 were mild, 31 were moderately severe and 5 were very severe. Myocarditis may occur at any time in the course of the illness, but is most common in the latter days of the acute stage or early in convalescence. Other complications seemed to increase the incidence of myocarditis. It was observed more frequently in the early years of life. Pericarditis was present in 3 cases or 17 per cent. Two of these patients died. Endocarditis was present in 4 cases or 0.22 per cent. Systolic murmurs at the apex were frequently heard, but were usually regarded as functional or relative. The low percentage

of endocarditis as compared with the percentages in several other series may be due to the milder type of scarlet fever in which the case mortality was less than 4 per cent. Unless it was very severe old heart disease does not necessarily indicate a serious prognosis in scarlet fever.

A Note on the Occurrence of Congenital Atrio-ventricular Dissociation.—CARTER and HOWLAND (*Bull. Johns Hopkins Hosp.*, October, 1920) report a case at five years of age. A cardiac lesion had been noted at nine months. At the age of two years an electrocardiographic record showed complete heart block. Two years later the diagnosis was confirmed by a different physician. The patient has never experienced shortness of breath, cyanosis, or given any evidence of an impaired myocardium although she plays around as other children do. An electrocardiographic record made in May, 1919, showed complete atrio-ventricular dissociation with an auricular rate of 103 and a ventricular rate of 37. The cardiac rate at that time was from 48 to 52 beats per minute. Seven other cases have been reported in the literature. The diagnoses were made at the ages of seven days to fifteen years. Of these 8 cases, including the present, 3 gave no symptoms; 1 had syncopal attacks; 2 had pain around the heart; 1 had dyspnea and palpitation on exertion; the present case had an occasional stitch in the side on exertion. Six cases had complete dissociation. One case had partial 2 : 1 rhythm. Another had alternating 2 : 1 rhythm and complete dissociation. Marked cardiac hypertrophy was present in 5, and slight in 3. All the cases were free from cyanosis except 1.

Hypopituitarism.—LISSNER (*Endocrinology*, July–September, 1920) reports the case of a child of twenty-three months, who was normal until the ninth month. At that time he began to gain rapidly in weight. Symptoms began with convulsions of flexor type, and these continued up to within one month of his death. There was no diabetes or glandular trouble in the family. The eyes showed edema of the retina but the throat was negative. There was a marked muscular dystrophy with profound facial cyanosis, diminutive external genitalis, doubling of weight in the third year, low sugar tolerance and an antemortem temperature of 107.5°. The roentgen-ray of the skull showed a small sella turcica. At autopsy the sella turcica was found to be small with the anterior and posterior clinoid processes underdeveloped. The pituitary body was present but underdeveloped. This showed the line of demarcation between the anterior and posterior lobes lost. Histologically numerous thin walled bloodvessels formed a plexus surrounding strands of polyhedral cells arranged in three or four rows. These cells were of the usual two types found in this gland, and they intermingled without definite arrangement or regularity, the "chief" cells being far more numerous. Here and there were a few follicles lined by low columnar epithelium. There was an abundance of loose connective tissue.

Amyotonia Congenita.—HOLMES (*Am. Jour. Dis. Children*, November, 1920) reports a case which conforms in all the essential details to the condition described by Oppenheim. The condition was present at birth. There was no permanent improvement, and the child died of the

usual pulmonary complications at the age of eighteen weeks. The significant lesions are found in the spinal cord and in the muscles. The spinal cord is relatively large for the age of the child; the anterior roots are diminished in size as compared with the posterior roots. There is no disturbance of the contour of the cord in cross-section. Microscopic examination shows complete absence of any acute or chronic inflammatory process, and no evidence of recent degeneration. Myelinization is normal. The cells of Clark's column are of normal size and well preserved. The large or motor cells of the anterior horns are strikingly few in number, and are in part represented by cells that are much smaller in size but otherwise of the same appearance. A cell of normal size is found only infrequently, but except in size such cells as are found are perfectly normal in appearance. There is no gliosis. In the muscles, areas or bundles of hypertrophied but otherwise normal muscle fibers are intermingled with areas of small apparently healthy muscle fibers. The latter appear to represent less fully developed bundles of muscle fibers. There is no evidence found of past or present degenerative processes. The component muscle cells are embryonic in appearance, resembling most closely muscle cells from a human fetus of the third month. There is no increase in connective tissue and no evidence of replacement of muscle tissue by adipose tissue. The histopathological findings are best explained on the assumption of a delayed or retarded embryological development affecting certain motor cells of the anterior horns and certain groups of developing muscle cells. No anomaly of muscle spindles, peripheral nerves, or bloodvessels is recognized.

The Effect of Diphtheria Antitoxin in Preventing the Lodgment and Growth of the Diphtheria Bacillus in the Nasal Passages of Animals.—GELIEN, MOSS and GUTHRIE (*Bull. Johns Hopkins Hospital*, November, 1920) publish the results of their experiments in animals. They say that certain conditions in their experiments with animals were quite different from those present in human beings. This is especially true of the frequency with which the carrier state occurs spontaneously and the ease with which it may be produced experimentally. In a large series of human beings including both children and adults, they found that a single examination revealed an incidence of diphtheria bacillus carriers of about 3.55 per cent. A second examination practically doubled the number of carriers discovered, while a third examination still further increased the original number. Among the 72 animals which formed the basis of these experiments, as well as the 40 additional animals which were also used in other experiments, none showed diphtheria bacilli at the beginning of the study. The investigators were able to induce the carrier state in man experimentally both with virulent and non-virulent diphtheria bacilli. This was not the result in all efforts but occurred in a considerable number of cases. In guinea-pigs, rabbits and cats they found the carrier state difficult to produce, and generally very transient if it occurred at all. In the 70 animals 358 cultures were made. It was found that the production of nasal infection or infestation of cats, rabbits and guinea-pigs was very inconstant even when the organisms were introduced directly into the nose. A somewhat higher percentage of animals showed positive cultures among those directly inoculated than among those merely exposed to a

carrier. Cats and rabbits became infected with about the same frequency, and the incidence of the positive cultures was almost similar. Among the guinea-pigs 66 per cent developed positive cultures, and 26 per cent of the total number of cultures showed Klebs-Loeffler bacilli. The duration of infection was usually quite short. The health of the animals was apparently unaffected by the mere presence of bacilli in the nose. The occurrence and duration of infection were independent of the virulence of the strain of organisms used, and were wholly unaffected by previous administration of antitoxin.

OBSTETRICS

UNDER THE CHARGE OF

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Inevitable Abortion.—VALLIER (*Rev. Argent. de Obst. Y. Gynec.*, 1920, iv, 10) considers these cases with regard to the presence or absence of fever. If rise of temperature has not developed, the indication is favorable, but where fever occurs it is an evidence that infection has reached the uterine cavity and that the lining membrane of the uterus has become involved. The development of symptoms during the third and fourth day results from growth of bacteria which reaches its highest point from the seventh to the ninth day of the puerperal period. Against this process the lochia discharge has some antiseptic power, leukocytosis may aid excessive formation and granulation tissue may limit absorption and prevent the spread of bacteria. If the blood is involved the patient will have rigors and evidence of septic embolism and thrombosis will soon become apparent. Treatment can do no good and the patient's recovery will depend entirely upon the degree of virulence shown by the invading germs. After fever has developed no treatment should be applied within the genital canal and even the finger should be excluded. The best method of emptying the uterus consists in stimulating the uterine muscles to contract which the writer does by the application of cold over the abdomen and the administration of quinin. No interference whatever is practised in the genital tract. If the contents of the uterus are not discharged nothing is done until the fever has subsided, then the uterus should be curetted. If the patient has free bleeding operation is forbidden and if the uterus becomes retroflexed it must first be put in favorable position before it can be emptied. KING (*Jour. Am. Med. Assn.*, 1920, No. 75, p. 147) does not interfere with the genital tract in treating infections after labor or abortion. A very careful bimanual examination is made and if possible a culture obtained from the uterine cavity. If there is reason to believe that a portion of the placenta has not been delivered, this is removed with the least possible disturbance. The patient is placed practically in the Fowler position to secure drainage. High

temperature is modified by the use of water. The patient is given fluids very freely by bowel or the stomach and in some cases beneath the skin or in the vein, and enemata are employed to empty the intestines. If nausea develops it is often relieved by calomel, cold over the abdomen in the acute stage and later copious douches of hot water seems to be of value, such douches can only be given after the acute symptoms have subsided. In choosing the time for operation it is useful to examine cultures from the womb and when they are negative and fever has disappeared, the indications for operation are favorable. Immediate interference may be made necessary by the presence of pieces of placenta in the neck of the womb or by free hemorrhage caused by the retention of a portion of the embryo within the uterus. In 33 patients who had well-marked infection of the blood 8 died, of whom 2 were dying when brought to the hospital. Twenty-three of these cases had pelvic cellulitis develop but in 17 this entirely cleared up, 4 of them had late formation of pus and 2 died after interference which was evidently not indicated. Four patients died from active infection of the peritoneum. There were 266 abortions complete or incomplete in which all the patients made an entire recovery. Of these 86 had some disturbance of temperature. These cases had been followed up and some of them have had healthy pregnancies and natural birth. So far as can be ascertained operations have been performed upon none.

Fatal Cases in Puerperal Period from Sepsis of Other than Puerperal Origin. — From the Clinic of Würzburg, SCHMITT (*Monatschr. f. Geb.*, 1920, No. 2, vol. li) reports cases ending fatally from an infection of non-puerperal character, in 20,000 cases of labor in thirty years. There were 5 deaths from puerperal infection following normal labors; 1 of these patients had gonorrhea and had received local treatment up to the time of labor. Two had infection of the blood stream originating in the tonsils and 2 had infection with exogenous germs introduced during digital examination. In these cases the infection was evidently autogenous. Most writers upon the subject had admitted the possibility of autogenous infection by which is meant a general puerperal infection from bacteria present in the genital tract before labor. In these cases bacteria from the lower infected portion of the genital tract make their way upward and enter the uterus. Von Rosthorn first called our attention to puerperal infection from the blood stream. Experiments and clinical observations have shown in 12 carefully studied cases that in 8 the pneumococcus was the infecting germ, in 1 a streptococcus from pneumonia and in another polyarthritis from staphylococcus. In 1 typhoid ulcerations from the intestines and in another the Streptococcus angina. In recent literature there have been reported additional cases of Streptococcus anginosis, 2 of which had origin in the tonsils from which bacteria entered the blood. In the 20,000 labor cases in the Würzburg Clinic 1 of these cases was the only instance of infection developing in the blood stream. The writer describes the case of a primipara, aged twenty-three, who had a normal labor without lacerations. On the fourth day she had chill and fever and on the seventh day had pain in the throat, both tonsils reddened and swollen. The

lochia was normal, the abdomen normal, the uterus not sensitive. On the eighth day the abdomen became distended, on the ninth day peristalsis ceased in the intestines and on the tenth day death ensued. Autopsy showed a purulent pus streptococcus, peritonitis and swollen spleen and apparent parenchymatous degeneration of the liver and intestines. There was no pus in the uterus although the uterine muscle was slightly yellow in color. At the placental site there were small red granulations but no sign of infection. Vessels in the broad ligament were not involved and there was no purulent lymphangitis. The left tonsil was red and greatly swollen, the right was not reddened but swollen and boggy. No bacteria were obtained in the endometrium nor any evidence of infection in the uterus. On microscopic examination pus taken from the peritoneum was swarming with streptococci, from the tonsil streptococci were apparently not present, on making section of the tonsil the characteristic changes produced by infection were found. There could be no question concerning the relation of the process in the tonsil and the fatal result in the patient. We have abundant examples of infection in the other serous membranes of the body for which the focus existed in some comparatively distant organ, but cases of genuine peritonitis following foci in other organs than the abdomen are not common. The second case had also a normal labor but was examined internally three times by students. The first seven days of the puerperal period were normal, but the patient developed high temperature on the eighth day with pain in the upper portion of the left thigh, and in the lower third of the thigh marked swelling and sensitiveness. The patient died on the twelfth day with symptoms of general sepsis. A thorough autopsy failed to reveal evidence of infection in the genital tract nor were the blood-vessels in the genital region involved. On the inner aspect of the left thigh there was a bleb filled with blood, and the connective tissue in this vicinity was infiltrated with bloody fluid. Evidently there had been some lesion in the thigh which had produced the general infection. The third patient had normal labor. On the fourth day she had violent pain in the back and right upper thigh. On the fifth day fever, then chill, with normal lochia and sensitiveness on the right side of the abdomen. On the sixth day distention and on the seventh evidence of acute peritonitis. Operation was performed, the intestines were distended, the fluid in the peritoneal cavity containing streptococci. Drainage was introduced, the intestines became paralyzed and the patient died on the fourteenth day. The vessels in the parametria showed pus, thrombosis of the right femoral veins, the bronchi were greatly reddened, swollen and the right lung adherent to the pericardium. In the lymphatic glands of the region there was dark blackish-red hemorrhage. The uterus, tubes and ovaries were normal. On careful questioning it was found that just before coming to the Clinic for labor the patient had nursed her sister suffering from a severe attack of influenza. The fourth patient came to the Clinic because a child was ill with scarlatina at home. On admission she was isolated and not examined and labor occurred three hours after admission. Chills and fever developed on the fourth day without other symptoms. On the sixth day the lochia became foul and there was tenderness on both sides of the uterus. On the eighth day peri-

tonitis and on the tenth day death without signs of scarlatina. Unfortunately an autopsy could not be obtained. In the reviewer's experience fatal streptococcus infection followed delivery of a patient at which the operator was assisted by a physician who was in constant attendance upon a severe case of scarlet fever. Careful antiseptic precautions were taken during the delivery, the operator not knowing at the time that the assistant was in attendance upon the case of scarlet fever. This fact was concealed as long as possible but the death of the patient and natural questioning as to the possible source of the infection revealed the true circumstances. The reviewer observed a primipara with spontaneous labor, followed on the fourth or fifth day by considerable fever. The genital tract showed no evidence of infection, careful examination of the mouth revealed tenderness at the root of a partly decayed tooth. A dentist incised the gum obtaining about 1 dram of very foul pus, a disinfection of this area was followed by prompt disappearance of the fever and uninterrupted recovery of the patient. In a third case in the experience of the reviewer death followed Cesarean section. At autopsy the genital tract was in an aseptic condition, intestinal mucous membrane was greatly reddened and swollen with areas of ulcerations and lymphangitis in the peritoneum and intestines. The history revealed the fact that before coming to hospital the patient had tried to destroy the child by taking large doses of violent and irritant cathartics. In the absence of other evidence it was concluded that infection had arisen in the intestinal tract and had been the cause of death.

The Moisture and Ash of Maternal and Fetal Blood.—STANDER and TYLER (*Surg., Gynec. and Obst.*, September, 1920) published the report of their studies on this subject in the obstetric clinic of the Medical School of Yale University. After stating in detail in tables the results of their work, they find that during pregnancy the water-content of the blood is usually from 77 to 82 per cent of normal. The tendency is toward the larger quantity and this was even exceeded in one-third of the cases. If patients are examined month by month during pregnancy, considerable changes in the water of the blood are found. Until the seventh month, this greatly increases, then remains stationary or slowly decreases. By the time that labor begins it is practically the same as in the early weeks of gestation. Labor itself seems to have no constant influence upon the quantity of water in the blood. The water-content of the blood varies inversely with the corpuscular count. The water in blood plasma, examined month by month, shows the same kind of changes which are found in the whole blood. During pregnancy, so far as quantitative analysis is concerned, the ash of the blood and the ash of the plasma remain normal. So far as blood moisture is concerned, one cannot distinguish eclampsia from nephritis. In both the percentage of water may be sufficient to constitute a true hydremia and this is often seen in patients having marked general edema. When the ash in maternal and fetal plasma indicates that a free exchange of inorganic material is taking place, the proportions of each are identical, and this change is going on through the placenta by the process of osmosis. Moisture of the whole blood is considerably higher in the mother than in the fetus. The moistures

in mother and child approach each other closely, although a difference of 1 per cent in favor of the fetus is generally found. Factors not clearly known keep up osmotic change between the circulation of the mother and child and water passes through the placenta equally well in either direction.

GYNECOLOGY

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Vaginal Cysts.—The clinical importance of vaginal cysts is not extensive, neither are they of extreme rarity: their interest lies chiefly in their origin, for which there are several possibilities. In presenting this subject STRONG (*Am. Jour. Obst. and Gynec.*, 1921, i, 357) reminds us that traumatism or operative enclosure may result in a cyst without characteristic features. More interesting are heterotopic vestibular or cervical glands which may give rise to cysts of the lower or upper vagina. Apart from such misplacement of the glands it must be noted that the squamosa of the vagina may, through faulty development, be replaced by columnar epithelium and this may give rise to glandular structures which may become cystic. Vaginal cysts from such an origin are liable to be small, multiple, with a low columnar epithelium which may be in true papillæ. The most interesting form of cysts, is that derived from the Wolffian or Gärtner's duct, and this type may be of considerable size. It is interesting in point of size, in point of complexity of form, and in its predilection site, but apart from these considerations it must be admitted that origin from the Wolffian duct is largely inferential and that there is no determining characteristic. There are three sites of predilection of vaginal cysts, namely, the epoöphoron, the ampulla and the lowest portion of the vagina inclusive of hymen. Abnormalities in form and course of the ducts occur. The epithelium is so variable and individual that one can hardly speak of true abnormalities, and squamous epithelium has been found in adults. Cysts are the commonest variations from the persisting duct and occur in various sites. Finally adenocarcinoma and adenomyoma may be formed from rests.

Gehrung Pessary for Cystocele.—The advantages and method of use of the Gehrung pessary in the relief of cystocele has been emphasized by ILL (*Am. Jour. Obst. and Gynec.*, 1921, i, 338) who reminds us that the pessary consists of the Hodge instrument bent on itself so as to

form a double horseshoe, one lever being a little shorter than the other. Its object is to hold up the anterior wall of the vagina and, with it, the bladder. The position of the pessary is such that the smaller horseshoe or lever will be placed anterior and below the cervix, while the larger one will be just above the neck of the bladder. The junction of the two horseshoes will remain in both lateral fornices. To fit well the pessary should be freely movable and not felt by the patient on walking or sitting down. In fact she should not be conscious of wearing the instrument except that she is comfortable, that she has lost the dragging sensation and the irritable bladder. The introduction of the instrument is rather difficult to describe. The pessary is held between the thumb and the fingers of the right hand by the rounded end of the horseshoe, the smaller one being forward. The connection between the horseshoe to the patient's left is introduced first and then with a rotary motion of 180 degrees the whole pessary is slipped into the vagina where another rotation of 180 degrees will put it in place. Care should be taken that neither horseshoe slips behind the cervix in which case it will have to be removed and reintroduced, for the cervix will form a bar over which the pessary cannot be slipped. It goes without saying that experience and trial can only determine the proper size of the instrument to be used for each case. It is better to start with a small-sized pessary and allow the patient to walk about the office as a test, than to use a large instrument which may produce pain and injury. Ill states that those who will take the trouble and patience to master it will find great satisfaction for themselves and secure immeasurable relief for their patients. The great objection to the pessary is that while the patient can remove it she cannot replace it, Gehrung to the contrary notwithstanding.

Roentgen Treatment of Uterine Hemorrhage.—KINNEY (*Calif. St. Jour. Med.*, 1921, xix, 76) very wisely remarks that uterine hemorrhage is a presenting symptom, never a diagnosis, and the underlying pathology must be ascertained before any intelligent treatment can be instituted. In approaching a case of prolonged atypical hemorrhage one must eliminate, first, the accidents and incidents of pregnancy, second, pelvic infection, and third, malignancy. Having ruled out this triad, practically every case of uterine hemorrhage can be controlled by roentgenotherapy. However, efficient roentgen-ray treatment involves the establishment of the menopause and sterility and, therefore, the roentgen-ray will only be called into use after the general physical and mechanical conditions have been ruled out or properly treated. There are cases on record where the ovaries have been protected during roentgen-ray treatment and normal menstruation and normal pregnancy have followed a clinical cure. However, the danger of the complete arrest of menstruation limits the roentgen-ray treatment of uterine hemorrhage to those conditions where the establishment of the menopause is justifiable. Kinney has found roentgenotherapy efficient and suitable in the following types of cases: (1) In patients that have atypical bleeding from a grossly normal uterus nearing the menopause or as incident of the menopause the hemorrhage can be controlled and the menopause established in practically 100 per cent of cases. (2) In uterine hemorrhage from small fibroids at or near the menopause the

arrest of the bleeding and establishment of the menopause are certain, and the fibroid will disappear or decrease in size and become symptomless. (3) Patients that are poor surgical risks with uterine hemorrhage from any type of fibroid can be relieved from their symptoms of hemorrhage quickly and effectually by roentgen-ray. (4) There are certain cases where uterine hemorrhage and dysmenorrhea are so destroying to the patient's emotional and mental balance or so undermining her physical condition that a menopause is justifiable, and where it is justifiable it can be secured easily and certainly with roentgenotherapy. On the other hand, roentgenotherapy is contra-indicated where the establishment of a menopause is not justifiable, and is contra-indicated in the treatment of uterine hemorrhage where that hemorrhage is a symptom of an urgently surgical condition. Uterine hemorrhage in adolescence can be readily controlled without danger by radium and it is not justifiable to assume the risk of the menopause except where radium is not obtainable or in extreme cases. In the hemorrhage of uterine fibroids in young women the patients should be given a chance of a myomectomy if possible rather than hazard their expectancy of motherhood. Uterine hemorrhage accompanying a submucous of sloughing fibroid is the presenting symptom of a distinctly surgical condition and should only be treated as such. The treatment of large fibroids with symptoms of pressure can be successfully carried out with roentgen-ray and is justifiable in those cases presenting serious surgical contra-indications. But whether the roentgen treatment of large fibroids in patients that are good surgical risks is justifiable is still an open question. Kinney does not believe that it is justifiable and considers that the extirpation should be strongly advised for every patient having a large fibroid or with definite pressure symptoms. Furthermore, uterine hemorrhage with malignancy is an indication for either radium or surgery, and one must be constantly on guard to see that these cases have their radium or their surgery at the earliest possible moment. The foregoing statements and opinions are as fair and unbiassed as any we have ever known to come from a roentgenologist.

Primary Pelvic Lymphadenitis.—Although no little study has been given to the lymphatic glands of the pelvis from both the anatomical and the clinical standpoint, such investigations have been practically limited to the consideration of these glands in malignant disease of the uterus or other pelvic organs. The possibility of non-malignant disease of these glands, as well as that of primary malignant, lymphatic disease seems to have been overlooked. The occurrence of 3 cases of enlargement of the pelvic glands giving rose to striking clinical manifestations during a two months' service had led WILLIAMS (*Boston Med. and Surg. Jour.*, 1921, clxxxiv, 194) to believe that pelvic masses consisting of such glandular enlargement must be of not infrequent occurrence although but seldom recognized. The term primary disease of the pelvic lymphatic glands is, perhaps, somewhat inaccurate inasmuch as, with the sole exception of lymphosarcoma or Hodgkin's disease, involvement of any part of the lymphatic tract must be secondary to a process in some other organ or tissue. He has selected the title, however, to differentiate those cases in which the enlargement of the glands in itself gives rise to important clinical manifestations, from those in

which the enlargement of the glands is solely a measure of the extent of a malignant process in another organ. An analysis of the cases which Williams has observed shows that a mass in the pelvis close to the pelvic brim and definitely not connected with the uterus or its appendages was present in all 3 cases. Pain was present in all 3 cases. In 2 it was localized in the right iliac fossa and in 1 it was localized along the course of the ureter and in the kidney region and was due to occlusion of the ureter by pressure of the glandular mass from without. Psoas spasm was present in 2 of the 3 cases and must be regarded as quite an important symptom. Of course a roentgen-ray of the spine is necessary to rule out the mass and contracture due to psoas abscess from spinal caries. The leukocyte count in all these cases, even the 1 with abscess, ranged between 9000 and 11,600. Further observations may or may not reveal higher white counts in more virulent infections. The white count, obviously, must be influenced in great part by the particular organism concerned as well as the resistance of the patient.

Enormous Ovarian Cyst.—A case of an ovarian cyst which weighed more than the patient who carried it has been reported by HARLEY (*Indian Med. Gaz.*, 1921, lvi, 18) and reminds us of the type of cases that were quite prevalent before the day when Ephraim McDowell showed the way to the medical profession by performing his classic ovariotomy. In the case reported by Harley, the patient had noticed an enlarged abdomen over a period of fifteen years and at the time of operation she weighed 246 pounds, while immediately after operation she only weighed 82 pounds. Thus the tumor and its contents weighed 164 pounds or twice as much as the patient herself. It is unfortunate that the patient did not survive the operation, although it could hardly be expected that she would have much resistance when in such a physical condition.

Results of Radiation in Benign Conditions of Uterus.—As a result of a follow-up investigation in a series of 58 cases of benign pathological conditions of the uterus which were subjected to radium therapy, PAYNE (*Virginia Med. Monthly*, 1921, xlvii, 525) is convinced that radium is the treatment of choice in all cases of small myomata whose only symptom is hemorrhage and in all types of myopathic hemorrhage and in all types of uncomplicated leukorrhea. In his work he noticed that immediate cessation of the periods occurred in about 40 per cent of the cases: two or more periods in about 23 per cent of the cases: a return to normal with regular periods in about 15 per cent of the cases. In about 5 per cent of those cases in which immediate cessation of the bleeding occurred, there has been a return after a period of about one year which has been readily controlled with a second dose of radium. There is usually a profuse leucorrheal discharge following large doses of radium in about 19 per cent of the cases and a slight leucorrheal discharge continuing for about six to eight weeks in about 26 per cent of the cases. Pain coming on after the third day and lasting about a week occurred in about 25 per cent of the cases. In women above forty years of age or in those cases where larger doses have been given, about 50 per cent of them showed symptoms of the menopause following their treatment.

Gynecologic Backache.—In a series of 721 cases of backache studied at the Woman's Hospital in New York by BULLARD (*Am. Jour. Obst. and Gynec.*, 1921, i, 717), 85 per cent were cured by an appropriate operation. About 15 per cent of this series having one or more common gynecologic causes of backache present were not relieved of the backache by anatomically satisfactory operations, but probably much more than 15 per cent of female backache is not gynecologic. This series suggests that 15 or 20 per cent of all women with retroversion, prolapse, pelvic inflammations, obstetric lacerations or pelvic tumors do not have backache. Bullard pleads for closer coöperation with the orthopedist, the internist and the neurologist in order that the gynecologist may better diagnose and treat backache in women.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Russell's Fuchsin Bodies.—In the course of a study of dental granulomas, MCCONNELL and LANG (*Jour. Med. Research*, 1920–21, xlii, 99), made a careful examination of the fuchsin bodies found in these lesions. The granulomas studied consisted in a chronic or subacute process occurring between the tooth and the surrounding bony tissue, characterized by marked infiltration of plasma cells, with fuchsin bodies occurring in close relation with them. By oil immersion objective, it was apparent that the fuchsin bodies had their origin in the plasma cells, minute droplets being seen in the cells which showed the characteristic staining reactions. The authors consider that they result from degenerative changes taking place within the protoplasm of the cell, in which the nucleus takes no part. No one type of cell can be considered as the sole origin, as no type of nucleated cells can be ruled out. Brown and others believe that fuchsin bodies arise from red blood cells, but the authors think that the evidence is against this, since there was found to be no relationship between fuchsin bodies and capillary channels, no association with hemorrhage, no indication of changes in the red cells and that they show different staining reactions from red cells, being intensely Gram-positive.

Transmission of Specific Immune Bodies from the Mother to the Young.—HOWELL and EBY (*Jour. Infect. Dis.*, 1920, xxvii, 550), conducted an interesting series of experiments upon six rabbits to demonstrate, (1) the transmission of specific immune substances from the

mother to her offspring; (2) the duration of immune bodies in the serum of off-spring of immune rabbits and (3) the effect of parturition upon the antibody-content of the serum of an immune rabbit. Rabbit 1, was immunized against human red blood cells; rabbit 2, against sheep red blood cells; rabbits 3, 4, 5, and 6 were immunized against streptococcus viridans, Type II pneumococcus, meningococcus and B. typhosus respectively. The results were concisely epitomized in tables. The principles gleaned from the experiments led the workers to conclude that there is considerable variation in the antibody content in the serum of rabbits. The agglutinin and complement-fixation bodies were apparently more stable in the instance of rabbit 6 which was immunized against B. typhosus than in the remainder. The workers demonstrated that complement-fixation antibodies generally were less stable than the hemolysins, agglutinins and opsonins studied in this series. Concerning the original hypothesis, the workers feel that there is a definite transmission of specific immune bodies from mother to offspring, but they are not prepared to state from these experiments the source of these immune bodies, whether from maternal circulation or from mother's milk, and that the duration of the specific immune bodies in the serum of the young is only four to six weeks and ever decreasing in amount. The proof is furnished by the tests that parturition produces a definite decrease in the antibody content of the maternal serum.

Studies on Measles. I. Susceptibility of Monkeys to the Virus of Measles.—In an attempt to arrive at more conclusive evidence concerning the susceptibility of animals to the virus of measles, BLAKE and TRASK (*Jour. Exper. Med.*, 1921, xxxiii, 385), presented the results of several interesting and fruitful experiments on the transmission of this disease from man to monkeys and the passage of the infection from monkey to monkey. Of 10 monkeys inoculated with both filtered and unfiltered nasopharyngeal washings from seven patients with measles, 8, after an incubation period of six to ten days, developed symptoms closely resembling those of measles in man. The secretions from the human cases of measles were collected by irrigation of the nasopharynx with 20 to 40 c.c. of sterile 0.85 per cent salt solution. Five to 10 c.c. of the nasopharyngeal washings were introduced intratracheally into the monkeys. The symptoms which the animals presented were constant and consisted in listlessness and drowsiness after a definite incubation period (averaging seven days), catarrhal conjunctivitis, a characteristic enanthem usually confined to the labial mucous membrane, a definite exanthem consisting of discrete, red maculopapules constant in character but somewhat variable in extent and duration, and comparable histologically with the lesions of measles, a leukopenia and prompt and complete recovery after an illness of seven to ten days' duration. It was further shown that the characteristic group of symptoms which followed the inoculation of monkeys with the nasopharyngeal washings from patients with measles could be successfully carried through six passages by intratracheal injections of saline emulsions of the skin and buccal mucous membranes of monkeys killed from two to six days after the onset of the symptoms. From the fourth passage monkey the reaction was also successfully induced in 3 monkeys

by means of citrated whole blood injected intravenously. It was found that the blood so introduced was capable of inciting the reaction from at least the seventh to thirteenth days after intratracheal inoculation of the donor monkey but incapable of inducing it from the second to fourth days. Cultures of the blood showed no growth. The incubation period after the intravenous injection of blood was shorter than when intratracheal instillations of the nasopharyngeal secretions were employed, being four instead of seven days. From their experiments the authors conclude that Macacus rhesus monkeys are susceptible to inoculation with the virus of measles.

Hemolytic Streptococci of the Appendix Vermiformis.—KRAFT (*Jour. Infect. Dis.*, 1921, xxviii, 122) comments on the paucity of information at hand on the etiological significance of the hemolytic streptococci in appendicitis. He investigated 48 normal and 77 pathological appendices removed at operation, with the object of determining the frequency with which hemolytic streptococci are found in the normal appendix and in acute and chronic appendicitis, and if possible, the role they play as a primary etiological factor in appendicitis. The organisms were cultured from the appendiceal contents, the mucosa and wall of appendix, being classified according to Holman. Two strains of streptococcus hemolyticus infrequens were isolated from 48 apparently normal appendices where they occurred only in small numbers. Three strains of Streptococcus hemolyticus infrequens and 1 of streptococcus hemolyticus II occurred in 77 pathological appendices in almost pure culture. The acute appendices yielding hemolytic streptococci were either ulcerated or gangrenous. No hemolytic streptococci were isolated from 25 chronic appendices. All strains of hemolytic streptococci isolated were pathogenic for rabbits. A review of other work shows that hemolytic streptococci are frequently encountered in the gastro-intestinal tract. In acute appendicitis, however, it appears that hemolytic streptococci when present are the predominant organisms and the principal etiological agent. Thirty-two strains of Streptococcus viridans were isolated from 48 normal appendices. Of 108 strains of non-hemolytic colon bacilli which were encountered 45 were found in the 48 normal appendices and 63 in the 77 pathological appendices; 51 strains of hemolytic colon bacilli were isolated of which 19 were found in 48 normal appendices. Two probably pneumococcus strains were found, also 1 case of pin worm. In addition, many large unidentified bacilli, which, in all probability, were non-pathogenic were found.

Diphtheria Carriers and Wound Diphtheria.—SIMMONS, WEARN and WILLIAMS (*Jour. Infect. Dis.*, 1921, xxviii, 327) report 75 cases of diphtheria and 102 diphtheria carriers occurring at the Walter Reed General Hospital from October, 1918 to August, 1919. All active cases and carriers were isolated. Schick tests were performed on all contacts, and when indicated, these contacts were immunized with diphtheria toxin-antitoxin mixture. All active cases received antitoxin. Throat carriers were treated with various antiseptic solutions and tonsillectomy was performed in selected instances. The average period of isolation was twenty-two days, varying in individual cases from six days to

six months. The character of treatment appeared to play but little part in removal of the diphtheria bacilli, except that in 6 cases tonsillectomy abolished the carrier state in a comparatively short time. Local applications did not effect wound diphtheria carriers to any appreciable extent. Two of the 5 cases of active wound diphtheria died. Of 52 strains tested, 48.1 per cent from contact carriers, 42.8 per cent from wound carriers, 80 per cent from active wound cases and 84.6 per cent from convalescent carriers were virulent for guinea-pigs. Without exception, the organisms conformed to the typical morphological to cultural characteristics of B. diphtheriæ. Neither morphology, fermentation reactions nor other cultural characteristics gave any indication of the degree of virulence of the organisms studied.

Diphtheria Carriers and their Treatment with Mercurochrome.—GRAY AND MEYER (*Jour. Infect. Dis.*, 1921, xxviii, 323) found that in examining 680 individuals, routinely, 23.8 per cent harbored diphtheria bacilli. The majority of positive cultures were secured from the nasal passages. Ninety carriers were treated systemically by dropping, spraying or swabbing with an aqueous solution of mercurochrome—220, in 0.5 to 2.0 per cent strength. Eighty-eight of the 90 were made carrier-free by an average of 19.1 treatments, the remaining 2 resisting all treatment.

HYGIENE AND PUBLIC HEALTH

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DIRECTOR OF HYGIENIC LABORATORY, UNITED STATES PUBLIC HEALTH SERVICE, WASHINGTON, D. C.

The Heat Resistance of Spores with Special Reference to the Spores of Bacillus Botulinus.—WEISS (*Jour. Infect. Dis.*, 1921, xxviii, 70) states that the free spores of Bacillus botulinus are destroyed within five hours at 100° C., within forty minutes at 105° C., and within six minutes at 120° C. Bath temperatures are indicated. These thermal death points were determined under optimum conditions for survival. The destruction of the spore is a gradual process, not an instantaneous killing and is probably due to a gradual protein coagulation. The spores are evidently injured before they are killed. This is inferred from the fact that the more protracted the period of heating, before killing occurs, the longer the period required for the spore to vegetate. Young moist spores have a higher thermal resistance than old moist spores. Spores that are one month old are found to be three

times as resistant as spores that are five months old. There is a general decrease in thermal resistance as the spore ages. The more resistant individuals change more rapidly than the less resistant ones causing a tendency toward stabilization, the ultimate resistance of the individual more nearly approximating the average resistance. This is shown by the effect of dilution on the thermal resistance of young and old spores, the old spore emulsions being practically unaffected by changes in the number of spores present, while the young spore emulsions show marked decrease in resistance as the dilution increases. The thermal resistance of emulsions of young spores increases as the concentration of the emulsion increases. Sodium chloride considerably lowers the thermal resistance and the rate of this lowering increases rapidly as the concentration of the salt is increased. The hydrogen ion lowers the thermal resistance of the spore and the rate of this reduction decreases as the hydrogen-ion concentration increases. The hydroxyl ion lowers the thermal resistance and the rate of the reduction decreases as the hydroxyl-ion concentration increases. The hydrogen-ion concentration changes considerably in a medium in which Bacillus botulinus is growing and ultimately stabilizes itself at a point near a PH value of 7.5. In applying these results to the practical problems of processing canned foods, it is necessary to determine the PH value of the material to be sterilized immediately before the exposure. Any delay between the determination and the processing may cause a sufficient change in the PH value to require a higher temperature or a longer period of exposure. In all practical processing methods a sufficient safety factor should be allowed. The actual time required in applying such a factor becomes rapidly less as the temperature of processing is increased. Thus, a 50 per cent safety factor applied at a processing temperature of 100° C., the medium to be sterilized having a PH value of 7, would require an extra heating of sixty minutes or a total of one hundred and eighty minutes. The same safety factor applied at a processing temperature of 120° C., the medium to be sterilized being the same, would require an extra heating of three minutes or a total of nine minutes.

Studies on the Relation of Mineral Dusts to Tuberculosis. I. The Relatively Early Lesions in Experimental Pneumokoniosis Produced by Granite Inhalation and their Influence on Pulmonary Tuberculosis.—GARDNER (*Am. Rev. Tuberc.*, 1920, iv, 734) used the R1 strain of tubercle bacillus to infect guinea-pigs by the inhalation method, coincidently and previously exposed to granite dust of a given concentration. He concluded that the occurrence of tubercles is more frequent in the dusted than in the undusted lung. That such lesions tend to run a more prolonged course than those in animals not exposed to dust. That the spread of the tuberculous process to the regional lymph nodes is not prevented.

Experimental Studies of the Nasopharyngeal Secretions from Influenza Patients. I. Transmission Experiments with Nasopharyngeal Washings.—OLITSKY and GATES (*Jour. Exp. Med.*, 1921, 2, xxxiii, 125) state that they detected an active substance in 5 patients in early stages of epidemic influenza during 1918–19 and 2 patients in early

stages of epidemic influenza during 1920. It was not detected in 12 cases of the same disease in which the onset of obvious symptoms occurred more than thirty-six hours before washing of the nasopharynx was carried out nor was it found in the secretions of 14 individuals free from the syndrome of influenza either during the epidemics or the interval between them. With this substance a clinical and pathological condition has been induced in rabbits, affecting the blood and pulmonary structures mainly, which could be maintained and carried through at least fifteen successive animals. For this reason, and also because of the dilution between passages, they are led to believe that they were dealing with the actual transmission of a multiplying agent rather than with a passive transference of an original active substance. In some of the experiments secondary infections by ordinary bacteria were encountered. The relation of these microörganisms to this active substance will be dealt with later the authors state. However the essential effects were produced by a substance wholly unrelated to these bacteria. The similarity that exists between the effects produced in rabbits on the blood and the lungs and those occurring in man in epidemic influenza provides a basis for further investigation on the inciting agent of epidemic influenza.

Venereal Statistics of the Army and Navy.—Riggs (*U. S. Naval Med. Bull.*, No. 1, vol. xv) states that the normal expectancy for venereal disease resulting from illicit sexual intercourse not followed by prophylaxis is about 1 in 20 or 1 in 30. The expectancy for venereal disease when prophylaxis is used depends almost entirely upon the factor of time. The absence of the time factor in a set of prophylactic statistics invalidates any conclusion that may be drawn concerning probable efficiency of prophylaxis. In actual practice the number of infections appears to be reduced by nearly one-half. The questionnaire method of investigation, in which the identity of the individual is concealed, has proved unreliable and the results obtained cannot be accepted with any confidence as to their accuracy.

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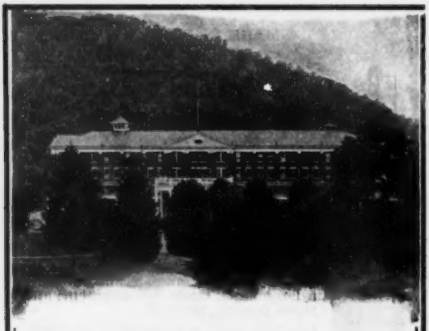

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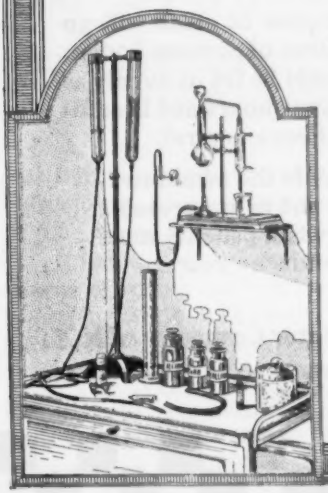

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